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THE HUMAN GROWTH CURVE: I. PRENATAL

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A. INTRODUCTION

One aim of the investigator studying growth is to obtain a governing law and thence to form generalizations. The theoretical equation, based on precepts and concepts of how the organism should grow, makes an attempt to gain insight into the mechanisms shaping the growth curve. The constants of this equation then take on meaning; they may be interpreted and given definitions, and the equation is said to be rational.

Although the original growth data stand alone, the fitting of an equation contracts the data to a manageable form. The shape of the growth curve may now be expressed by two or three numbers rather than by the entire mass of the data. This is particularly advantageous to any subsequent treatment of the growth data of many individuals, for example, to the attempt to determine the effect of nutrition, heredity, or environment on the rate of growth.

There is a particular advantage to fitting an equation to individual human growth data. With animals, the general interest is in how the species grows; but with humans, there is a special interest in how the individual grows. With animals, the so-called cross-sectional method, where the weights of many animals at different ages are averaged to yield the growth curve, is used; with humans, the so-called longitudinal method, where the growth of one individual is followed serially, is the method commonly adopted. Fitting an equation to longitudinal data yields, therefore, specific information (in the nature of growth constants) on the individual under study.

*I am indebted to Mr. R. V. D. Campbell for his assistance in preparing the manuscript as well as his many helpful suggestions; to Dr. A. A. Weech for suggestions, careful editing of the manuscript, and for kindly furnishing data on growth in body weight of his three children; to Dr. Howard Mason for the loan of data on growth in body weight from birth to puberty of two of his private patients; and to Mr. Kenneth W. Breeze for his careful preparation and lettering of the charts. I wish to acknowledge the kind help of Mr. R. S. Childs, Mr. D. I. Crandall, and Miss E. J. Burlison.

No paper on the human growth curve can properly be introduced without paying tribute to the efforts and prolific writings of Samuel Brody (1926; 1927a, b, c, d, e; 1928; 1930; 1937 and others). He has derived a rational and useful equation to describe the growth in weight of animals and plants, the multiplication of bacteria, the increase of populations, etc.; and has assessed their respective rates of growth, predicted mature weights, determined equivalence of age between individuals and between species, etc.; and thoroughly discussed the meaning of growth rates, concepts of growth, and other equations suggested to describe growth.

On the subject of the growth in weight of the embryo, the reader is referred to the thorough review by Needham (1931) who has given a clear discussion of empirical and theoretical equations proposed to describe the embryological growth of animals and man. He gives unprejudiced criticism of the generalizations derived by the various investigators from their particular equations.

Brody employs two essential ideas throughout his work: (*a*) that the rate of growth of the embryo and the rate of postnatal growth before the major inflection in the growth curve (before puberty, metamorphosis, etc.) is proportional to the growth already made,

$$\frac{dw}{dt} = kw \tag{1}$$

where $\frac{dw}{dt}$ represents the instantaneous rate of growth, w, the weight, and k, the proportionality constant, termed the "velocity constant" by Brody (1927a); and (*b*) that the rate of growth after the major inflection is proportional to the growth yet to be made,

$$\frac{dw}{dt} = k(A - w) \tag{2}$$

where $(A - w)$ is the amount of growth yet to be made, A being the mature weight (1927b). Brody has rationalized these expressions as extensions of the physico-chemical principle of mass action (1927).

It is the purpose of this and of the following paper to extend further these essential ideas of Brody's so as to embrace the curve of growth in body weight of the human (in particular) more fully than he has done.

A single equation which can be fitted to the entire growth curve has been derived by Wetzel (1933). Without wishing to detract from an ingenious and brilliant demonstration of the possibilities in this

direction, it must in all fairness be pointed out that the usefulness of such expressions is limited by their complexity, by the labor of fitting them to observational data, and by the paucity of data when the growth of individuals is under consideration. Since the environmental factors which modify growth may be expected to change with the passage of years, there is much reason for isolating some of the phases of growth. The environment of the fetus is wholly different from that of the infant; there is yet no evidence to show that the hereditary factors which modify growth at the age of puberty are operative during early childhood. Some of the features of "discontinuity of the growth curve" and the value of dealing with the curve in segments are discussed by Brody (1927).

The human growth curve in body weight from conception to maturity is made up as follows: first, an accelerating portion lasting until birth, the prenatal phase; a portion extending from birth to puberty in which the curve decelerates for about two years and then accelerates; lastly, a decelerating phase continuing to maturity.

Birth has been picked, in this work, as one of the divisions between phases since the weight curve has a discontinuity at this time. The individual usually loses weight for about three days after birth and regains the birth weight in from eight to fourteen days (Meredith, H. V., and A. W. Brown, 1939). From birth to puberty the course of growth in body weight, although made up of a decelerating and an accelerating portion, shows no discontinuity, and there is no physiological evidence of any modifying influence on the course of growth. At puberty, however, growth is influenced by the endocrine secretions. It is reasonable, then, to take as the second phase of the growth curve the period from birth to puberty. The third and last phase is that portion of the curve from puberty to maturity.

The first section deals only with the prenatal phase of growth. The section following deals with the human growth curve in body weight from birth to puberty. The phase of growth following puberty has been thoroughly dealt with by Brody (1927b, 1927d), and since this phase follows the extended line of thought to be presented here, no curves or data for this portion will be shown.

A study of the growth in body weight of the human fetus may appear to be too *gross* to yield anything definite on the actual transformation of the embryonic structures, whether cells or groups of cells, into the particular parts to which they are destined to give rise. But since growth in body weight (which also implies growth into a par-

ticular form) of the embryo is cellular self-multiplication, in which new cells arise from pre-existing cells, we should be able to determine quantitatively the rate of growth in body weight of the substance of the embryo which *as a whole* is giving rise to differentiated structures.

Further, we should be able to determine the governing law for the growth in body weight of the fetus *as a whole*, and from the nature of the law evaluate genetic constants for the species being studied.

The fundamental process with which we are concerned in a study of fetal growth is cell-multiplication. Our starting point, then, is the single cell which represents the union or fusion of two germ cells. This cell is potentially the exclusive source of the new cells of which the organism is composed. It is a simple step to state, as Brody does, that the total weight of the embryo at any time is proportional to or depends upon the amount or weight of the embryonic tissue already there, for cells arise only from pre-existing cells. But this statement is not enough to describe the growth of the embryo. It is but another simple step to state that the rate of growth in weight of the embryo is proportional to the weight already there *plus* some inherent (in tangible) growth-stimulating factor.

B. Fundamental Concept

This section and the one following are based on a fundamental concept of growth—an extension of Brody's original ideas: that the rate of growth *at any time in the life of the organism* is proportional to the "effective weight" for growth. This idea is symbolically written as,

$$\frac{dw}{dt} = kw' \tag{3}$$

where $\frac{dw}{dt}$ is the instantaneous rate of growth, w' is the "effective weight" for growth, and k is a proportionality constant.

Brody (1937) had already made use of a similar idea when he proposed that the metabolism is proportional, not to the weight of the individual, but to the "physiologic weight."

C. The Prenatal Growth Equation

Several equations have been suggested to describe the embryological portion of the growth curve. Brody (1927a) assumes that the rate of growth is proportional throughout to the growth already made

(Equation 1). This concept is useful since k, the fractional rate of growth, has a simple interpretation. But in order to describe the growth in weight of the fetus from about eight weeks after conception to birth, three equations are needed, each having different constants. Since the growth curve is smooth and continuous during this period, the division into three segments seems artificial.

Scammon and Calkins (1924, 1924a) obtained empirical equations for prenatal growth, the purpose of which was to predict the weight of the fetus from its age or from linear dimensions. In this respect an empirical equation which fits the data closely becomes very useful. It is, however, the aim of this paper to obtain an equation which fits the data and for which the constants may be given a simple interpretation.

Following the line of thought that the rate of growth at any time is proportional to the "effective weight" for growth, it is unreasonable to assume that the "effective weight" for growth at any time is identical with the actual weight. At conception the "effective weight" for growth may probably equal the actual weight of the egg (after fertilization) and for a time the course of growth may follow Brody's law $\frac{dw}{dt} = kw$, and one cell gives rise to two, two to four, four to eight, etc. However, this type of growth cannot persist. It seems plausible, as previously mentioned, that there may exist in the embryo an inherent "impulse to grow." Certainly, by the time the embryo has developed into a fetus there is the possibility of a more complicated type of growth. Organs have become differentiated and may be elaborating hormones capable of exerting a new influence on the course of growth. No longer is the "effective weight" for growth represented by the mere mass of fetal tissue. There is of course no certainty that the "impulse to grow" arises from reactions within the fetus nor that its arrival coincides with the transition of embryo into fetus. It may depend upon a factor originating outside the fetus, perhaps in the placenta. However, if this "impulse to grow," whatever it may be, is thought of as being equivalent to a given quantity of fetal tissue, having an effect on the rate of growth equivalent to an additional supply of tissue, we may express, symbolically, the concept for the rate of growth of the fetus as,

$$\frac{dw}{dt} = k(A + w) \tag{4}$$

where $\frac{dw}{dt}$ is the instantaneous rate of growth in weight per unit time $(A + w)$ is equal to w', the "effective weight" for growth, w is the weight at time t, k is a constant of proportionality, and A is the weight-equivalent of the "impulse to grow."

Equation 4 may be integrated,

$$\int \frac{dw}{A + w} = \int k dt$$

$$ln(A + w) = kt + lnB$$

where lnB is the constant of integration. Then

$$w = Be^{kt} - A \tag{5}$$

or

$$w = Ae^{k(t-t')} - A \tag{6}$$

where $B = Ae^{-kt'}$, so that t' is an age parameter indicating where the curve crosses the age axis, for when $t = t'$, $w = o$.

D. Fit of Experimental Data to Equation 6

Tables 1, 2, and 3 give Streeter's records (1920) of growth of the human fetus. The original data have been somewhat altered by

TABLE 1

The Growth in Weight of the Human Fetus (White Males) Taken from Streeter's Records (1920)

The original data have been somewhat altered by averaging over ten day intervals. Fetuses weighing 10 gms. or more: white males.

Age in days	Weight in gms.	No. of embryos averaged over-10-day intervals
83.9	15.0	19
95.3	37.1	15
104.6	72.0	19
114.8	124.9	23
123.5	181.8	11
134.7	269.8	19
144.6	360.6	12
154.9	470.6	15
164.7	591.2	9
175.8	735.7	8
184.0	852.3	7
191.5	976.4	4
206.3	1260.0	3
217.5	1511.0	2
224.3	1648.0	3
235.3	1924.0	3
242.0	2178.0	3
256.7	2545.0	3
266.0	2912.0	2
274.5	3241.0	4
280.0	3596.0	1

TABLE 2

THE GROWTH IN WEIGHT OF THE HUMAN FETUS (WHITE FEMALES) TAKEN FROM STREETER'S RECORDS (1920)

The original data have been somewhat altered by averaging over ten day intervals. Fetuses weighing 10 gms. or more: white females.

Age in days	Weight in gms.	No. of embryos averaged over-10-day intervals
86.2	17.7	25
95.6	38.8	14
105.0	74.2	29
114.1	119.9	17
125.8	199.8	13
134.5	265.5	14
146.0	382.3	13
153.9	461.4	11
163.4	555.0	10
174.0	713.1	8
180.0	790.0	1
198.0	1090.5	2
205.3	1220.3	3
218.0	1643.0	1
227.0	1900.0	1
236.5	1957.5	2
245.5	2302.0	2
254.0	2523.5	4
265.0	2832.5	2
276.5	3187.5	2
298.0	4298.0	1

TABLE 3

THE GROWTH IN WEIGHT OF THE HUMAN FETUS (NEGROES, BOTH SEXES COMBINED) TAKEN FROM STREETER'S RECORDS (1920)

The original data have been somewhat altered by averaging over ten day intervals. Fetuses weighing 10 gms. or more: Negroes, both sexes.

Age in days	Weight in gms.	No. of embryos averaged over-10-day intervals
83.0	13.4	2
93.6	29.2	8
105.0	68.6	8
114.3	132.9	10
123.2	179.3	9
134.1	263.2	16
145.3	370.3	9
153.8	458.2	5
163.8	581.8	10
174.1	713.0	8
185.0	870.8	4
192.8	1012.0	4
203.0	1184.5	2
213.0	1386.7	3
226.0	1742.2	5
234.8	1982.8	4
243.0	2134.5	2
254.3	2629.8	4
263.8	2843.6	5
275.5	3242.0	2
380.0	3775.0	2
294.0	4064.0	1

separating males, females and negroes, and by averaging the observations over 10-day intervals.

Figures 1a, 2a, 3a show the plots of the experimental data with

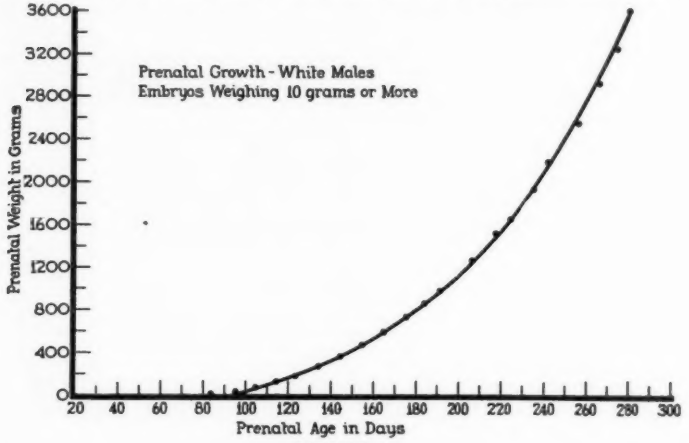

FIGURE 1a

FIT OF EQUATION 6 TO THE EXPERIMENTAL DATA SHOWN IN TABLE 1 FOR THE GROWTH IN WEIGHT OF THE HUMAN FETUS (WHITE MALES)

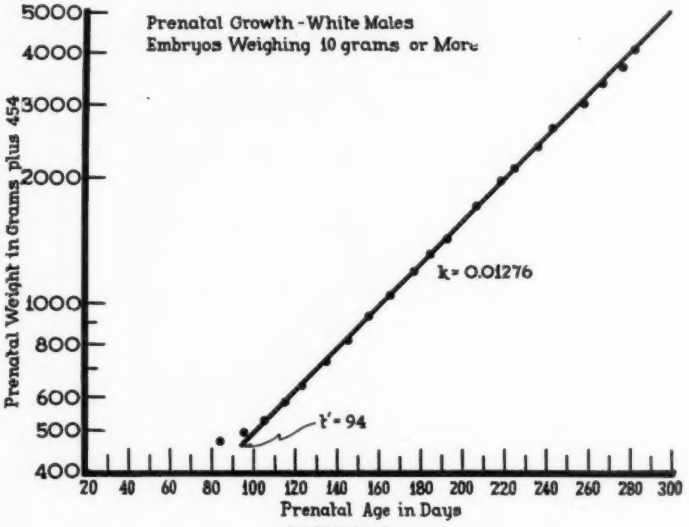

FIGURE 1b

THE CURVE IS A SEMI-LOGARITHMIC PLOT OF THE SAME DATA AND SMOOTH CURVE SHOWING ALL THE CONSTANTS

the smooth curve representing Equation 6 passed through. The same data and smooth curves are shown on semi-logarithmic charts in Figures 1b, 2b, and 3b in which $ln\ (A + w)$ is plotted against age, t.

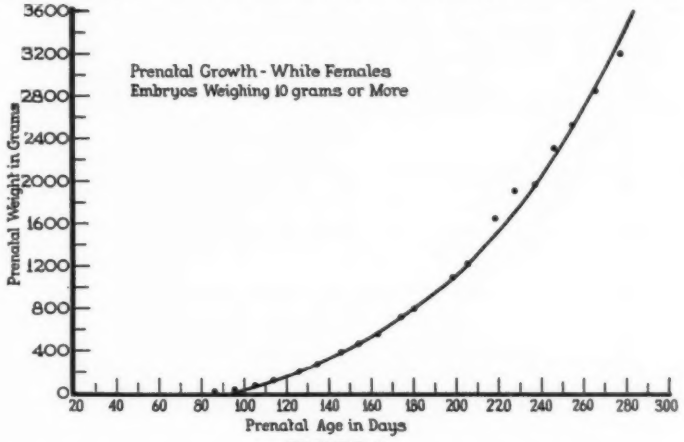

FIGURE 2a

FIT OF EQUATION 6 TO THE EXPERIMENTAL DATA SHOWN IN TABLE 2 FOR THE GROWTH IN WEIGHT OF THE HUMAN FETUS (WHITE FEMALES)

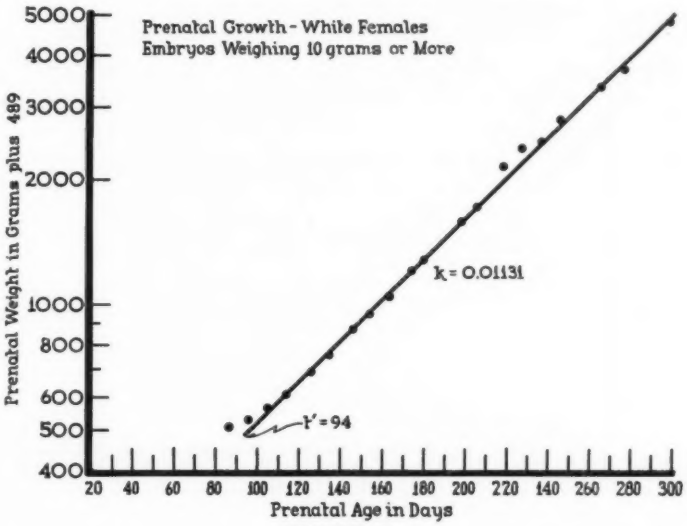

FIGURE 2b

THE CURVE IS A SEMI-LOGARITHMIC PLOT OF THE SAME DATA AND SMOOTH CURVE SHOWING ALL THE CONSTANTS

Table 4 gives a summary of the constants obtained for white males, white females, and negroes (both sexes combined).

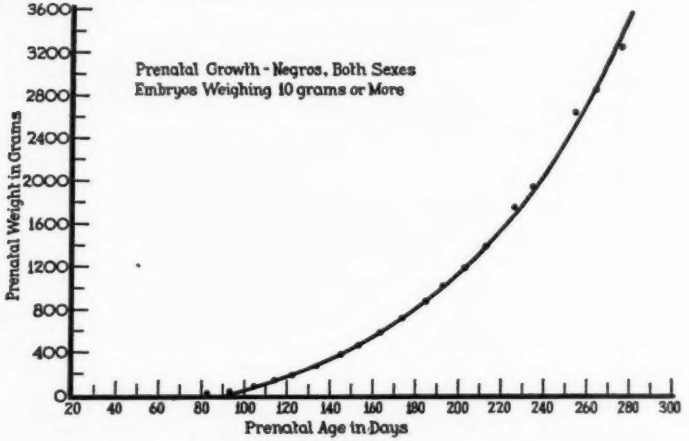

FIGURE 3a

FIT OF EQUATION 6 TO THE EXPERIMENTAL DATA SHOWN IN TABLE 3 FOR THE GROWTH IN WEIGHT OF THE HUMAN FETUS (NEGROES, BOTH SEXES COMBINED)

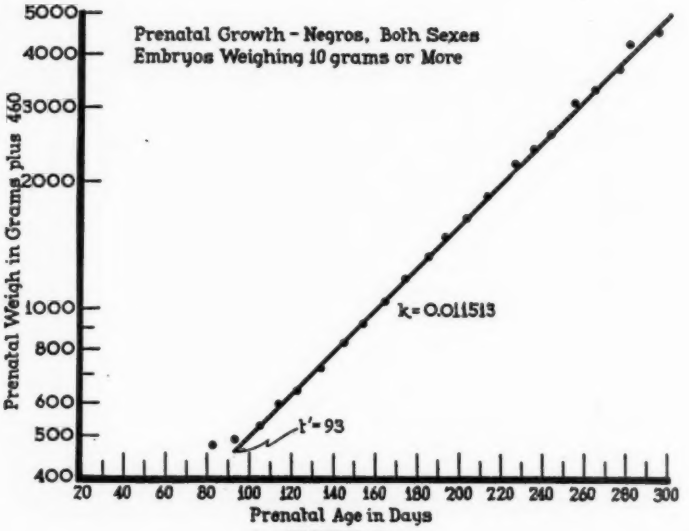

FIGURE 3b

THE UPPER CURVE IS A SEMI-LOGARITHMIC PLOT OF THE SAME DATA AND SMOOTH CURVE SHOWING ALL THE CONSTANTS

TABLE 4

SUMMARY OF THE CONSTANTS OF EQUATION 6 AS FITTED TO THE DATA FOR THE EMBRYONIC GROWTH OF MAN

	k % per day	A Grams	t' Days
White males	1.181	454	94
White females	1.131	489	94
Negroes, both sexes	1.151	460	93

The three constants in Equation 6 can be evaluated by choosing three points equally spaced on the time-axis and solving the three equations.[1] Another method is the following: if the constant A is chosen correctly by trial, the other two constants may be evaluated directly by plotting $ln\ (A + w)$ versus t. If the constant A is chosen too high, a curve upward will result, if too low, a curve downward will result, and if correct, a straight line will result.

Notice from Figures 1, 2, and 3 that the smooth curve crosses the age-axis at about three months of fetal life. At this age the cells are highly differentiated and the embryo has acquired its special organs. Before this time many new cells were produced, but the actual size of the embryo is negligible to the prenatal growth curve.

Figure 4 shows the fit of Equation 6 to the data, compiled by Needham (1931a), for the embryonic growth of a number of animals, introduced here for comparison with man. Needham's compilation gives the results of a number of investigators on one animal. For the purpose of this paper, the most complete data of any one investigator were chosen, or if more than one was equally complete for a given animal, the data were averaged. The following summarizes the data used: McDowell on the embryonic growth of the mouse; the averaged data of Murray, Schmalhausen, and Byerly on the chick; Hammond, Buchem, Bergmann, and Rorik on the cow; Stotsenberg on the albino rat; Draper on the guinea pig, averaged every five days;

[1]When three points equally spaced on the time axis (w_1, t_1), (w_2, t_2), (w_3, t_3), are chosen, the solutions for the three constants are,

$$A = \frac{w_2 - w_1 w_3}{w_1 + w_3 - 2w_2}$$

$$k = \frac{2ln\ \dfrac{w_2 - w_1}{w_3 - w_2}}{t_1 - t_2}$$

$$t' = t_1 - \frac{1}{k} ln \left(\frac{A + w_1}{A}\right)$$

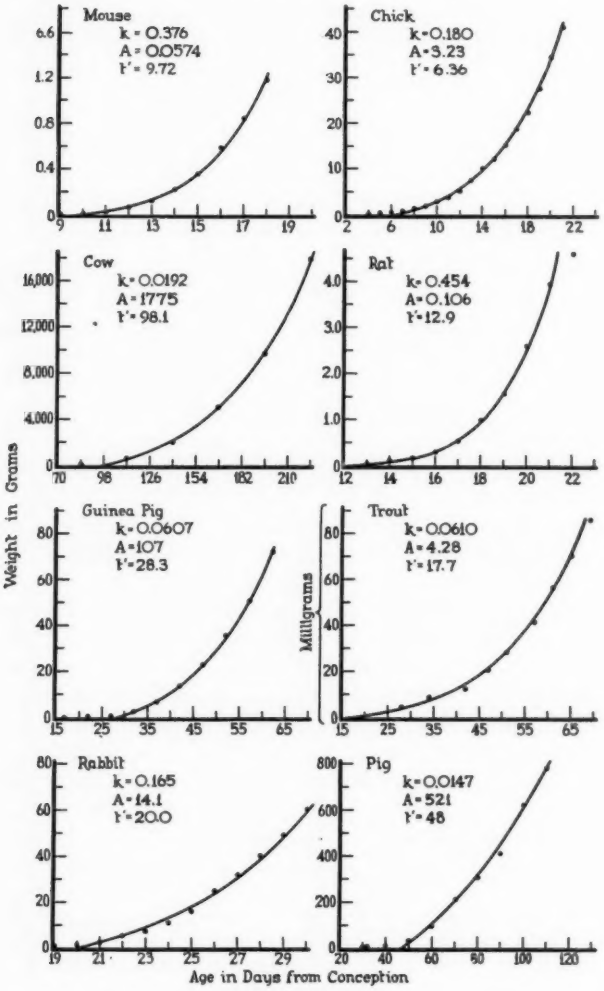

FIGURE 4

FIT OF EQUATION 6 TO THE EMBRYONIC GROWTH OF A NUMBER OF ANIMALS
The constants in the equation are shown on the chart.

Gray on the trout at 10° Centigrade; Chaine on the rabbit; and Warwick on the pig. The constants of the fitted equations (the

TABLE 5

SUMMARY OF THE CONSTANTS OF EQUATION 6 AS FITTED TO THE EMBRYONIC GROWTH OF A NUMBER OF ANIMALS

Animal	k % per day	A Grams	t' Days
Rat	45.39	0.1061	12.90
Mouse	37.59	0.0574	9.72
Chick	17.97	3.234	6.36
Rabbit	16.52	14.08	20.01
Trout	6.095	0.00428	17.68
Guinea pig	6.067	10.73	28.3
Cow	1.921	1775.0	98.1
Pig	1.472	521.3	48.0
Man	1.156	471.5	94.0

smooth curves) are given on the chart and summarized in Table 5.

Inspection of the growth curves for all of the animal embryos indicates that they too, like the curve for human growth, begin at a variable time period after conception. In the equations this time period is represented by t'. Other investigators who have noted the delay after conception before rapid growth begins have suggested that the phenomenon depends on the fact that the primitive streak does not appear until this time. Needham (1931) points out a conclusion reached by most investigators: that the general course of prenatal growth can be expressed by a relation between weight and age only when age is measured from the beginning of the embryo proper.

The present study confirms this conclusion without yielding additional facts to support or deny the possible explanations. In terms of the concept being developed the phenomenon is described by saying that in different animals the "weight-equivalent of the impulse to grow" manifests itself at some point in time after the egg is fertilized.

E. EQUIVALENCE OF AGE BETWEEN MAN AND ANIMALS IN THE GROWTH OF THE EMBRYO

Since the equation fitted to embryonic growth is an exponential equation, the equivalence of age between man and animals can be determined using Brody's technique (1927c): when $\frac{w}{A}$ is plotted against $k\,(t - t')$, using for each animal the respective values of A, k, and t', a single curve results with all the data about it. Without the exponential equation it is difficult to bring the various growth curves to a common basis. Figure 5a shows a chart of man and animals in

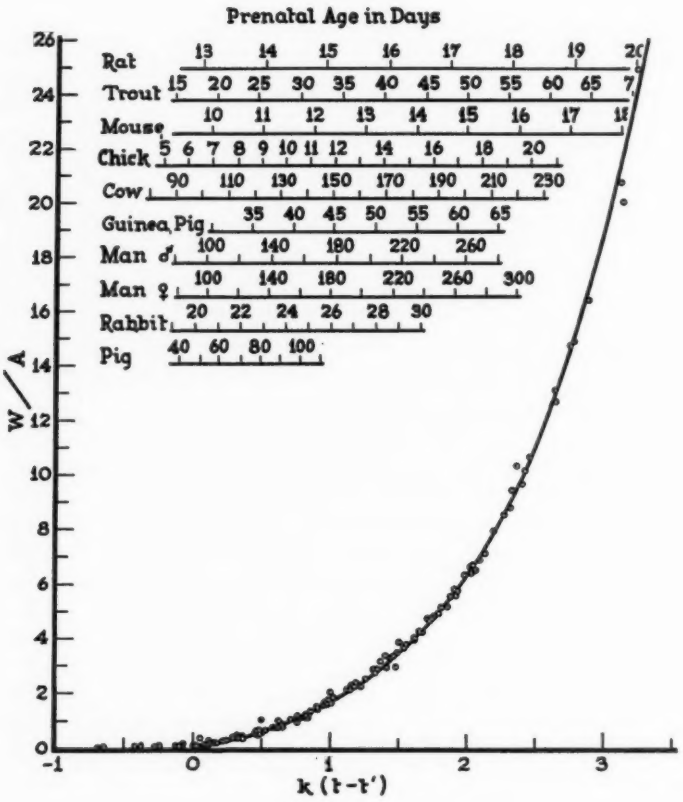

FIGURE 5a

EQUIVALENCE OF AGE IN EMBRYONIC GROWTH BETWEEN MAN AND ANIMALS

which $\frac{w}{A}$ is plotted against $k\ (t - t')$, then the appropriate age scales are laid off. Figure 5b is the same curve plotted on semi-logarithmic paper. It is put in here to show how well the prenatal growth of various animals obeys this law.

The equivalence of age between any two animals is given by the ratio of these respective k's. The order of the animals to accomplish a relative amount of embryonic growth equivalent to that of man in 100 days is: pig, 79; cow, 60; guinea pig, 19; trout, 19; rabbit, 7;

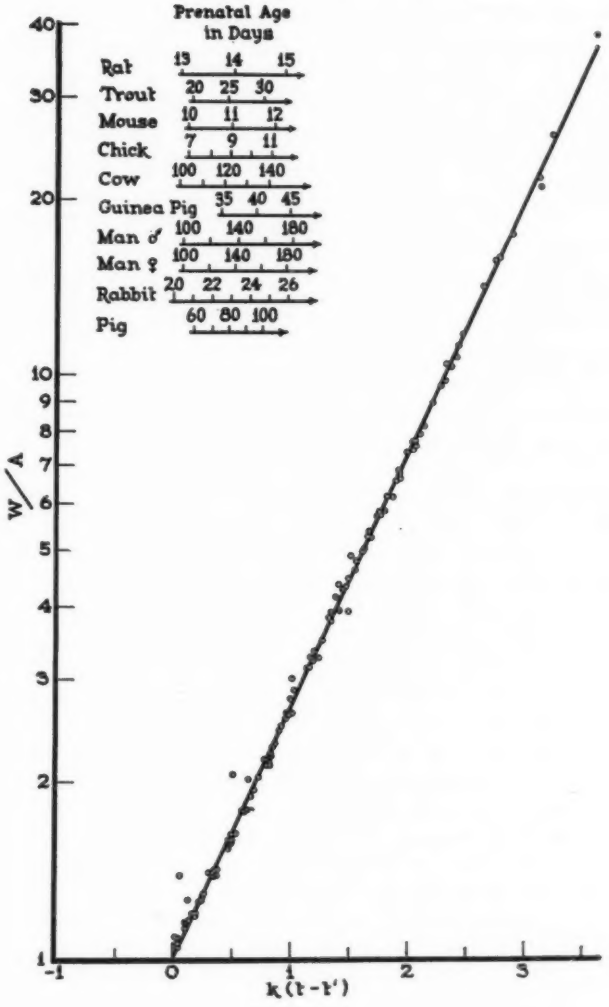

FIGURE 5b

THE CURVE IS A PLOT OF $\frac{w}{A}$ VERSUS $k\,(t - t')$ WITH THE APPROPRIATE AGE-SCALES LAID OFF

The upper curve is a semi-logarithmic plot of the same data and smooth curve showing the way all the animals studied fall upon this linear plot.

chick, 6; mouse, 3; and rat, 2.5. It must be remembered that the amount of growth is expressed in terms of A for each animal.

Note from Table 5 that the rate of growth, expressed by the value of k, of the human embryo is less than that of any of the other animals studied, and that, in general, the smaller the species the faster is its rate of growth and the smaller is the "weight-equivalent of the impulse to grow."

F. Summary

The general nature of the human growth curve in body weight is discussed, and the concept is proposed that the rate of growth at any time in the life of the organism—from conception to maturity—is proportional to the "effective weight" for growth. This concept yields a rational equation to which, in this first section, the prenatal growth of the human fetus and the prenatal growth of a few other animals have been fitted.

For the prenatal phase of growth, the "effective weight" for growth is represented by the actual weight of the embryo plus: some inherent "impulse to grow." In the equations this unknown quantity is represented by a weight-equivalent of the "impulse to grow," and is so determined from the data.

The human fetus has a slower rate of growth than any of the animals studied, the order being: human < pig < cow < guinea pig < trout < rabbit < chick < mouse < rat.

The exponential nature of the equation fitted to the growth of the embryo, $w = Ae^{k(t-t')} - A$, where w is the weight at age t, k is the "velocity constant," A is the weight-equivalent of the "impulse to grow," and t′ is the age after conception when rapid growth (in mass) begins, makes it possible to determine the equivalence of age between man and the other animals: 100 days in man is equivalent to 79 days in the pig; 60, cow; 19, guinea pig; 19, trout; 7, rabbit; 6, chick; 3, mouse; and 2.5 in the rat.

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THE HUMAN GROWTH CURVE: II. BIRTH TO PUBERTY

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A. SHAPE OF THE CURVE

The shape of the human growth curve from birth to puberty differs from that of any other animal, except possibly the other primates (Spence and Yerkes, 1937) in that the curve of growth in body weight is convex upward (growth decelerating) to about 2 or 3 years of age, then convex downward (growth accelerating) over a long period extending to puberty. After puberty the curve again becomes convex upward, growth is decelerating, and the curves of man and animals are similar (Brody, 1927).

No reasonably simple and rational expression describing the human curve from birth to puberty has been proposed. It is the purpose here to derive such an expression on the basis of concepts introduced in the preceding section.

B. THE GROWTH EQUATION FROM BIRTH TO PUBERTY

By assuming that growth is a form of motion, Wetzel (1937) has been able to apply the laws of mechanics to obtain an equation of growth. The properties which he ascribes to the organism are analogous to the mechanical properties of mass, resistance, and elasticity or to the electrical properties of inductance, resistance, and capacitance. By combining several constants the equation which he arrived at can be expressed in the following simplified form. His resulting equation

$$ln\, w = K_1 + K_2 e^{-K_3 t}\, cos\, (K_4 t + K_5) + K_6 e^{-K_7 t}\, sinh\, (K_8 t + K_9)$$

where w is the weight at time t, and the K's are constants, is too complex to be useful in many practical situations.

Two other investigators, Jenss and Bayley (1937), have proposed an empirical equation in an attempt to describe the course of growth during infancy. Their equation,

$$w = K_1 + K_2 t - e^{-K_3 t + K_4}$$

fits observational data to 4 or 6 years of life.

Davenport and Drager (1936) use the empirical equation,

$$w = e^{(K_1 + K_2 t + K_3 t^2)}$$

to represent the course of growth from birth to two years, and state that this is the best simple equation that will pass through the points.

In the preceding section the concept of "effective weight" for growth was introduced. This concept states that the rate of growth *at any time in the life of the organism* is proportional to the "effective weight" for growth. When growth is accelerating the "effective weight," w', is equal to the actual weight of the organism, w, plus the weight-equivalent, A, of an "impulse to grow." Symbolically written,

$$\frac{dw}{dt} = kw' = k(A + w) \tag{1}$$

where w is the weight at time t and k is a constant of proportionality. On integration this equation yields,

$$w = Be^{kt} - A \tag{2}$$

where B is a constant of integration.

Extending the concept to include decelerating growth, we may assume that the "effective weight" for growth is then equal to the growth yet to be made, so that,

$$\frac{dw}{dt} = kw' = k(A - w) \tag{3}$$

In this equation A may represent the weight towards which the tissues are striving, or the mature weight for the last phase of growth, so that $(A - w)$ represents the growth yet to be made. Integrating the above we obtain,

$$w = A - Be^{-kt} \tag{4}$$

where B again represents a constant of integration. Equations 3 and 4 are, of course, identical with Brody's equations for this type of growth.

The growth curve of man, as a multi-cellular organism, is the sum of the growth of all the individual cells or groups of cells (tissues) of which the organism is composed. Considering the human body to be made up of tissues which obey one or the other of the two preceding types of growth, i.e., self-accelerating growth or self-inhibiting growth, and letting w_1 be the total weight of all the accelerating tissues, and w_2, the weight of all the decelerating tissues, we have,

$$w_1 = B_1 e^{k_1 t} - A_1 \tag{5}$$

and

$$w_2 = A_2 - B_2 e^{-k_2 t} \tag{6}$$

The total weight, w, is the sum of w_1 and w_2, hence

$$w = w_1 + w_2$$

and

$$w = B_1 e^{k_1 t} - B_2 e^{-k_2 t} - A_1 + A_2 \tag{7}$$

Equation 7 should then represent the course of growth in total body weight from birth to about puberty. In the next subhead it will be shown that this equation may be further simplified.

It is wholly improbable that the different tissues which are accelerating in their growth would all have the same growth-constant, k_1, and that the different decelerating tissues would all have the same constant, k_2. Hence, it must be considered that k_1 and k_2 represent only the average properties of their respective groups of tissues.

Justification for the assumption that some tissues of the body are accelerating in their growth while others are decelerating may be found in the work of Harris, *et al.* (1930), who have found that various tissues in the body grow in different ways. The types of growth which they designate as *neural* and *genital* correspond, respectively, with our *decelerating* and *accelerating* types, while their *general* type is a combination of the two. In particular, it may be noted that the growth of the brain is an excellent example of the decelerating type of growth (Weinbach, 1938).

C. Evaluation of Constants and Fit of Equation 7 to the Human Growth Curve

If we set $D = A_2 - A_1$ Equation 7 becomes,

$$w = B_1 e^{k_1 t} - B_2 e^{-k_2 t} + D$$

Now, when t is large, $B_2 e^{-k_2 t}$ is negligible, and

$$w = B_1 e^{k_1 t} + D$$

If, however, logarithm w is plotted against t (t large), the average data for man (see next paragraph) follow closely a straight line (Figure 1). Therefore, D must be very small. If we assume that D is zero, the simplified equation for w becomes,

$$w = B_1 e^{k_1 t} - B_2 e^{-k_2 t} \tag{8}$$

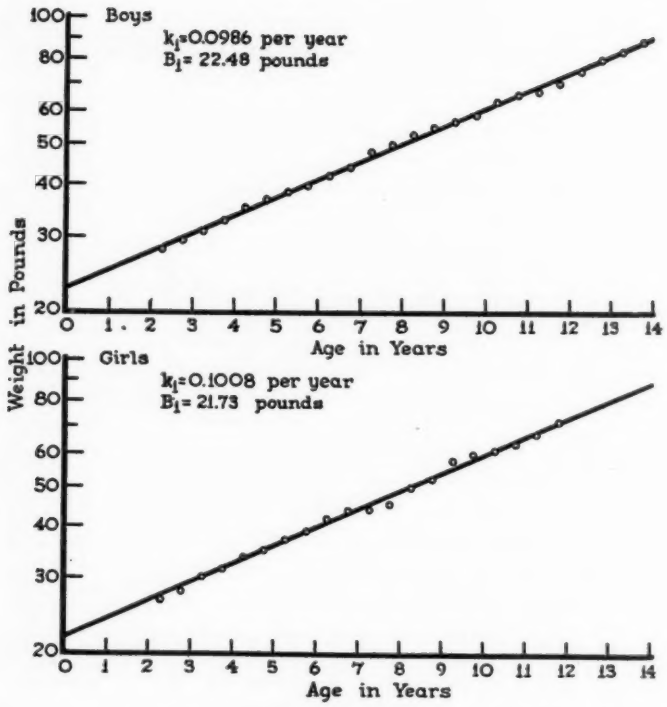

FIGURE 1

SEMI-LOGARITHMIC PLOT OF WEIGHT VERSUS AGE, I.E., $ln\ w$ VERSUS t, OF THE DATA ABOVE TWO YEARS SHOWN IN TABLE 1 FOR WHITE MALES AND WHITE FEMALES

The slope of the line is k_1 and the intercept on the weight-axis is B_1.

Since D is assumed to be zero, $A_2 = A_1$, or the weight to which the self-inhibiting tissues are striving equals the weight-equivalent of the "impulse to grow" of the self-accelerating tissues. The values of A_2 and A_1, cannot however, be exactly determined.

Table 1 gives the average data for the growth of man of Woodbury (1921), Palmer quoted from Boyd (1935) and Quételet quoted from Boyd (1935) to which Equation 8 has been fitted. The constants of the equation may be evaluated graphically: plot $ln\ w$ versus t, or w versus t on semi-logarithmic paper using only the weights above about two years, and draw a straight line through the data as shown in Figure 1. The slope of this line is k_1, and the intercept on the

TABLE 1

THE GROWTH IN WEIGHT OF THE HUMAN FROM BIRTH TO PUBERTY (WHITE MALES AND WHITE FEMALES)

The data from birth to two years are from Woodbury and after two years the data of Palmer and Quételet were averaged.

Age years	Males Weight pounds	Females Weight pounds	Age years	Males Weight pounds	Females Weight pounds
0.08	10.0	9.4	2.25	27.8	26.5
0.17	11.8	11.0	2.75	29.0	27.8
0.25	13.4	12.4	3.25	30.6	30.3
0.33	14.7	13.7	3.75	32.6	31.6
0.42	16.0	14.8	4.25	34.8	33.7
0.50	17.0	15.8	4.75	36.5	35.2
0.58	17.9	16.7	5.25	37.8	37.1
0.67	18.7	17.5	5.75	39.4	38.9
0.75	19.4	18.1	6.25	41.5	41.9
0.83	20.0	18.7	6.75	43.5	43.6
0.92	20.5	19.3	7.25	47.7	43.8
1.00	21.1	19.8	7.75	49.5	45.5
1.08	21.6	20.3	8.25	52.2	49.6
1.17	22.1	20.7	8.75	54.3	52.1
1.25	22.6	21.2	9.25	56.1	57.3
1.33	23.0	21.7	9.75	58.1	59.7
1.42	23.5	22.1	10.25	62.4	61.1
1.50	24.0	22.6	10.75	65.2	63.5
1.58	24.4	23.0	11.25	66.2	66.7
1.67	24.8	23.5	11.75	69.2	71.3
1.75	25.3	23.9	12.25	74.2	
1.83	25.7	24.3	12.75	79.2	
1.92	26.0	24.6	13.25	82.4	
2.00	26.4	25.0	13.75	87.3	

weight-axis is B_1. Calculate the quantity $B_1e^{k_1t} - w$ where w refers to the raw data below the age of about two years. Plot the logarithm of this quantity versus t, or use semi-logarithmic paper, and draw a straight line through the data as shown in Figure 2. Then k_2 is the slope of this line and B_2 is the intercept on the vertical axis.

Figure 3 shows the average data for males and females of Woodbury, Palmer, and Quételet plotted on cartesian coördinates to show the fit of Equation 8.

Figure 4 shows the fit of the equation to the individual data on growth in body weight from birth to about puberty of five girls and one boy, and Figure 5 shows a large number of children fitted by Equation 8. The data are shown in Tables 2 and 3.

D. FIT OF EQUATION 8 TO THE GROWTH CURVE OF THE CHIMPANZEE

As a point of interest, Equation 8 was fitted to the data of Spence and Yerkes (1937) on the growth in body weight of the chimpanzee. The data for one animal (Alpha) were chosen because they were

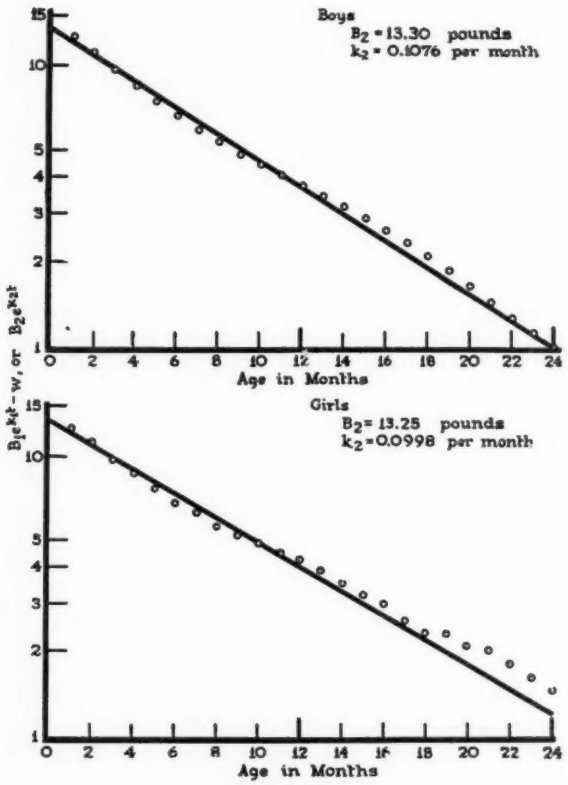

FIGURE 2

SEMI-LOGARITHMIC PLOT OF THE SMOOTH CURVE OF FIGURE 1 FROM BIRTH TO TWO YEARS MINUS THE DATA FOR THE GROWTH IN WEIGHT FROM BIRTH TO TWO YEARS SHOWN IN TABLE 1

The slope of the line is k_2 and the intercept on the vertical axis is B_2.

most complete from birth to puberty. Figure 6 shows the original data for the growth of Alpha with the smooth curve fitted to it as previously described.

As was remarked earlier, man and possibly the primates differ from all the other animals in the shape of their growth curves from birth to puberty. The other animals have a much shorter infantile period and show no deceleration in their growth just following birth. In view of the derivation of Equation 8, this difference may be

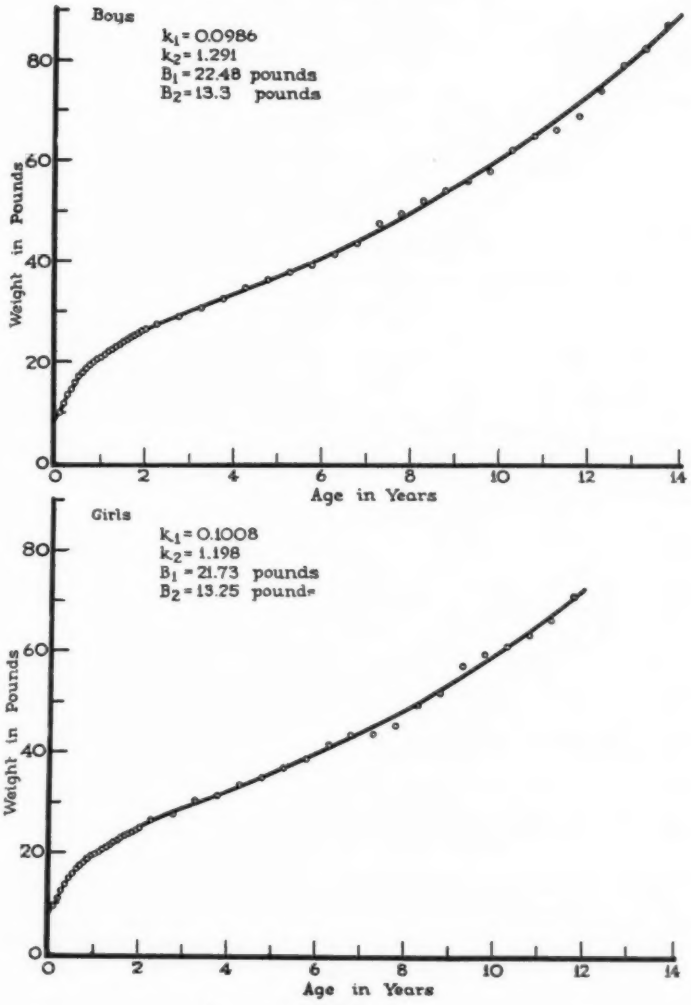

FIGURE 3

FIT OF EQUATION 8 TO THE EXPERIMENTAL DATA FOR THE GROWTH IN WEIGHT OF THE HUMAN (WHITE MALES AND WHITE FEMALES) OF WOODBURY, PALMER AND QUÉTELET AS GIVEN IN TABLE 1

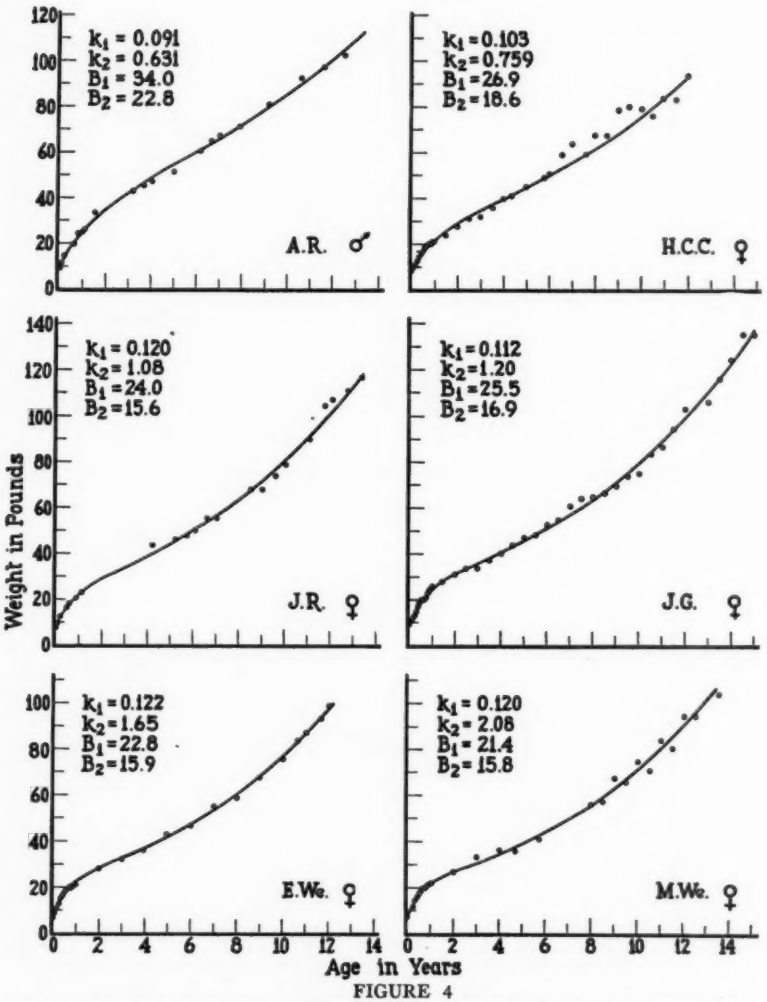

FIGURE 4

FIT OF EQUATION 8 TO THE INDIVIDUAL DATA ON GROWTH IN BODY WEIGHT FROM BIRTH TO ABOUT PUBERTY OF FIVE GIRLS AND ONE BOY

The data for the two girls, J. G. and H. C. C., were obtained from the report of Gray, H. and Faber, H. K. *Individual growth records of two healthy girls from birth to maturity. Amer. J. Dis. Child.*, 1940, **59**, 255-280. The data of M. W. and E. W. (sisters) were kindly furnished by their father, Dr. A. A. Weech, and the data of A. R. and J. R. (brother and sister) were kindly furnished by Dr. Howard Mason.

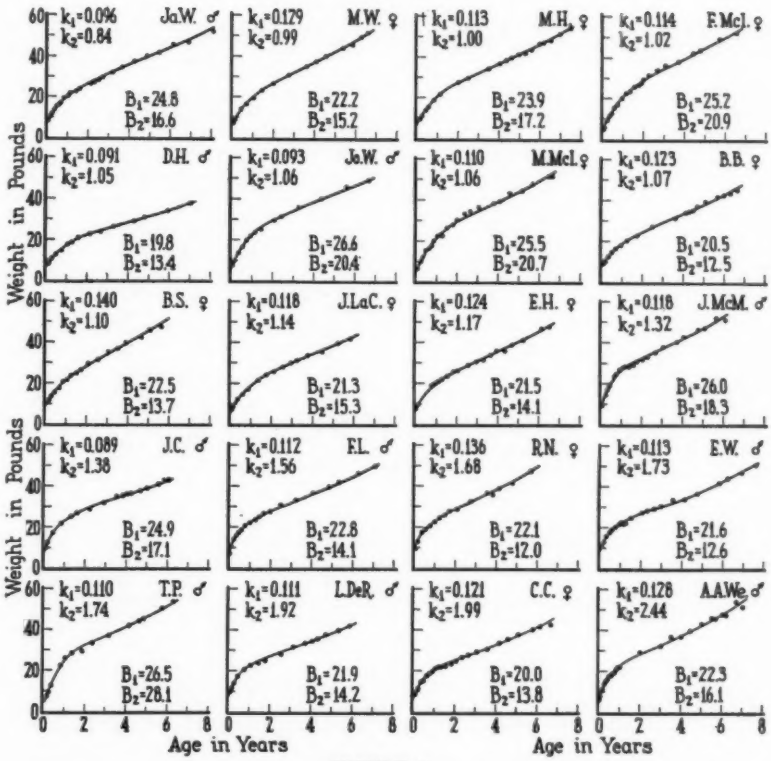

FIGURE 5

FIT OF EQUATION 8 TO THE INDIVIDUAL DATA ON GROWTH IN BODY WEIGHT FROM BIRTH TO ABOUT SEVEN YEARS OF 20 CHILDREN OBSERVED IN THIS LABORATORY

The curves are arranged in order of increasing k_2 reading from left to right.

attributed to either or both of two causes: the greater relative amounts of decelerating tissues in man and the primates, and, the slower growth of the accelerating tissues.

It is conceivable that man may have a greater relative amount of brain and nervous tissue than lower animals, and since the brain and nervous tissue seem to be of the self-inhibiting type, thus give rise to the initial bulge in the curve. However, this is highly problematical and a more reasonable explanation, substantiated by unpublished work in this laboratory, is that the initial convexity upwards is due to the relatively larger amount of fat in man during this period.

TABLE 2

THE GROWTH IN WEIGHT FROM BIRTH TO ABOUT PUBERTY OF THREE GIRLS AND ONE BOY

A. R.♂		*J. R.*♀		*E. We*♀		*M. We.*♀	
Age years	Weight pounds	Age years	Weight pounds	Age years	Weight pounds	Age years	Weight pounds
0.00	9.4	0.00	7.5	0.00	6.7	0.00	7.0
0.04	9.4	0.07	9.1	0.08	8.2	0.25	11.3
0.12	11.8	0.23	12.4	0.17	10.4	0.33	14.1
0.26	14.7	0.51	16.5	0.25	12.7	0.42	15.6
0.68	19.9	0.60	18.1	0.33	15.0	0.50	17.3
0.83	24.6	0.90	20.3	0.42	16.1	0.58	18.5
1.01	25.0	1.16	23.0	0.50	17.9	0.67	19.5
1.11	26.0	4.23	43.5	0.58	18.6	0.75	19.9
1.58	33.5	5.25	46.0	0.67	19.1	0.83	20.6
3.24	43.0	5.73	47.3	0.75	20.0	0.92	21.5
3.70	45.3	6.10	49.8	0.83	19.8	1.00	22.0
4.07	47.3	6.61	54.8	0.92	20.3	2.00	26.5
5.01	51.6	7.03	55.0	1.00	21.0	3.00	33.0
6.19	60.5	8.51	67.5	2.00	28.0	4.00	36.0
6.66	65.0	9.03	67.7	3.00	32.0	4.96	35.7
7.01	67.1	9.58	73.5	3.92	36.0	5.82	41.0
7.87	71.2	10.01	78.4	4.97	42.9	6.90	47.1
9.14	81.0	11.04	89.3	6.00	46.4	7.50	49.8
10.55	92.6	11.70	104.0	7.00	54.9	8.00	56.0
11.55	97.5	12.02	106.8	8.00	58.5	8.50	57.3
12.42	102.6	12.72	110.5	9.00	67.4	9.00	68.0
		13.28	116.3	10.00	75.5	9.50	65.6
				10.62	83.3	10.00	74.5
				11.00	87.0	10.50	70.7
				11.61	93.0	11.00	84.0
				12.00	98.9	11.50	80.5
						12.00	94.6
						12.50	94.3
						13.50	104.0

X-ray studies of the growth of muscle and fat on the forearm indicate that the fat follows closely the decelerating law of growth while the muscle is of the accelerating type. The bulge in the curve, then, may simply be due to the fact that man, with his long infantile period, is relatively inactive for the first year of life, and, compared to animals, more fat is deposited in preference to muscle growth. In Figures 4 and 5 it is interesting to note that the children (E. We., M. We., and A. A. We.) having the highest values of k_2, that is, having the largest initial bulges in their curves, are the children of a pediatrician and supposedly are under optimum nutrition, compared to the rest of the children in this study who are from families of marginal economic status.

E. THE MEANING OF k

Brody has termed k the "velocity constant" of growth. In the extended line of thought presented here, k, as a "velocity constant,"

TABLE 3

THE GROWTH IN WEIGHT FROM BIRTH TO ABOUT SEVEN YEARS OF 10 GIRLS AND 10 BOYS

Ja. W.♂		*M. W.* ♀		*M. H.*♀		*F. McI.*♀		*D. H.*♂	
Age years	Weight pounds	Age years	Weight pounds	Age years	Weight pounds	Age years	Weight pounds	Age years	Weight pounds
0.06	8.0	0.05	7.0	0.11	9.3	0.02	4.9	0.13	8.1
0.15	10.3	0.14	8.8	0.23	11.0	0.07	5.7	0.29	10.8
0.25	11.9	0.44	13.9	0.40	13.4	0.22	9.3	0.49	12.4
0.36	13.7	0.70	16.4	0.56	15.3	0.32	11.1	0.75	14.3
0.46	15.3	1.04	19.4	0.82	18.3	0.41	12.6	1.03	17.2
0.56	16.0	1.44	23.2	1.10	21.5	0.56	15.3	1.25	18.4
0.65	17.1	1.99	26.2	2.01	27.4	0.75	17.0	1.56	20.5
0.80	19.1	2.72	30.4	2.48	29.5	0.94	20.0	2.11	22.4
1.00	20.1	3.60	34.9	3.50	34.3	1.14	22.4	2.62	23.7
1.21	21.8	4.08	37.1	4.02	36.9	1.31	23.2	3.28	26.0
1.40	22.8	4.52	39.9	4.31	38.5	1.52	25.8	4.27	28.9
1.57	24.0	5.38	43.7	4.58	39.2	1.73	26.7	4.77	30.4
2.05	26.4	5.82	45.1	4.94	41.2	1.87	27.8	5.89	33.9
2.10	26.5	6.28	49.1	5.26	41.9	1.97	29.3	7.01	37.3
2.27	27.0	6.57	51.0	5.57	43.6	2.22	31.6		
2.48	28.1			5.94	46.6	2.61	34.3		
2.69	29.6			6.13	46.8	3.02	36.2		
3.03	32.0			6.50	48.0	3.67	38.2		
3.63	34.6			6.96	51.1	4.41	42.5		
4.22	37.4			7.48	54.0	4.74	43.9		
4.84	39.8					5.69	49.4		
5.41	41.4					6.51	52.2		
6.09	45.2								
6.84	46.8								
8.02	52.0								

TABLE 3 (*continued*)

Jo. W.♂		*M. McI.*♀		*B. B.*♀		*B. S.*♀		*J. LaC.*♀	
Age years	Weight pounds	Age years	Weight pounds	Age years	Weight pounds	Age years	Weight pounds	Age years	Weight pounds
0.06	7.3	0.07	6.2	0.11	9.1	0.17	11.7	0.08	7.4
0.15	9.6	0.22	10.0	0.16	10.1	0.28	13.6	0.13	8.8
0.34	13.4	0.34	12.0	0.32	12.4	0.43	15.2	0.34	12.2
0.54	16.1	0.47	15.2	0.50	14.6	0.68	17.8	0.60	14.8
0.73	19.6	0.61	16.7	0.69	16.1	0.87	20.4	0.88	17.2
0.91	21.3	0.75	17.8	0.94	18.1	1.06	21.8	1.37	21.6
1.13	23.1	0.89	20.0	1.23	20.1	1.25	23.5	1.75	24.1
1.42	24.9	1.03	22.2	1.72	22.9	1.47	24.9	1.98	25.8
2.08	29.1	1.17	22.8	2.48	27.2	1.71	26.2	2.55	28.0
2.41	31.0	1.30	22.3	3.56	31.4	2.08	29.4	2.93	29.7
3.26	35.7	1.50	26.2	4.08	34.0	2.54	31.3	3.13	30.5
4.36	39.9	1.79	27.9	4.26	34.5	3.06	35.0	3.75	33.5
5.56	45.4	2.00	30.1	4.45	35.1	3.50	36.4	4.44	35.3
6.63	48.9	2.36	33.2	4.65	37.0	3.91	39.2	5.22	39.3
7.69	53.5	2.61	34.3	5.06	39.5	4.61	42.2	5.82	41.8
		3.02	36.5	5.63	41.8	5.04	45.7		
		3.79	38.5	5.94	42.6	5.60	47.1		
		4.06	39.3	6.25	43.5				
		4.57	43.4	6.60	45.0				
		5.14	44.7						
		5.65	47.9						
		6.44	51.3						
		6.60	51.7						

TABLE 3 (*continued*)

E. H.♀		*J. McM.*♂		*J. C.*♂		*F. L.*♂		*R. N.*♀	
Age years	Weight pounds	Age years	Weight pounds	Age years	Weight pounds	Age years	Weight pounds	Age years	Weight pounds
0.00	7.2	0.08	9.0	0.11	10.0	0.02	7.1	0.06	9.6
0.11	9.1	0.22	14.0	0.20	12.4	0.10	10.7	0.16	12.7
0.77	18.8	0.33	16.9	0.46	17.1	0.21	14.0	0.36	17.2
0.84	19.0	0.43	18.7	0.83	21.3	0.33	15.9	0.53	18.7
0.99	19.9	0.67	23.3	1.23	24.9	0.46	17.2	0.79	20.4
1.12	20.9	0.74	24.2	1.63	26.6	0.60	18.3	0.99	22.3
1.26	21.3	0.90	26.5	2.22	28.6	0.78	20.6	1.22	24.1
1.54	23.2	1.08	27.5	2.90	31.8	1.00	21.9	1.46	25.7
1.81	25.3	1.17	28.0	3.52	34.7	1.28	23.3	1.70	27.6
2.04	26.0	1.34	27.8	3.84	35.1	1.46	24.9	2.08	28.3
2.55	28.5	1.59	28.7	4.04	36.0	1.67	26.2	2.77	32.1
2.95	30.2	1.76	30.4	4.24	36.1	1.98	27.1	3.51	36.2
3.30	31.1	2.03	31.5	4.70	37.5	2.49	30.3	3.81	35.3
3.62	33.2	2.28	32.8	5.00	38.6	3.22	32.9	4.13	38.6
3.95	35.6	2.63	35.0	5.58	40.7	4.05	36.1	4.76	41.1
4.33	35.9	3.00	37.3	5.82	42.4	4.85	39.1	5.58	47.0
4.68	38.8	3.69	39.9	6.08	42.9	5.31	41.3		
5.22	40.9	4.00	42.2			6.27	45.7		
6.12	46.3	4.71	45.9			7.04	49.1		
6.49	47.4	5.05	46.7						
		5.60	51.5						
		6.06	50.6						

TABLE 3 (*continued*)

E. W.♂		*T. P.*♂		*L. DeR.*♂		*C. C.*♀		*A. A. We.*♂	
Age years	Weight pounds	Age years	Weight pounds	Age years	Weight pounds	Age years	Weight pounds	Age years	Weight pounds
0.10	11.0	0.13	7.5	0.08	9.6	0.10	8.7	0.00	5.9
0.20	13.0	0.28	9.7	0.16	11.5	0.22	11.3	0.08	7.7
0.34	15.7	0.36	12.8	0.28	13.8	0.36	14.5	0.17	11.1
0.48	17.6	0.81	22.4	0.45	17.0	0.47	16.1	0.25	13.4
0.60	18.9	1.07	25.9	0.77	20.2	0.62	17.6	0.33	14.9
0.75	20.0	1.37	28.1	1.08	22.4	0.76	18.8	0.42	16.0
0.92	21.3	1.82	29.3	1.45	23.7	0.90	19.8	0.50	17.2
1.04	22.1	2.34	33.5	1.76	25.0	1.04	21.1	0.58	17.6
1.15	21.6	3.16	37.0	2.50	28.0	1.20	21.6	0.67	18.5
1.26	22.0	4.12	42.0	3.14	31.3	1.31	21.7	0.75	19.0
1.51	24.6	4.61	44.1	3.71	33.2	1.54	22.1	0.83	20.5
1.75	26.4	4.86	45.1	4.05	34.2	1.81	23.1	0.92	21.3
2.06	27.1	5.74	50.3	4.33	35.3	2.02	24.6	1.00	22.0
2.31	28.0	6.28	53.6	4.70	37.3	2.32	26.3	2.00	29.0
2.63	29.0			5.32	39.6	2.62	27.8	3.00	32.0
2.97	30.4			5.87	41.7	3.04	29.1	3.51	36.5
3.50	33.2					3.54	30.6	4.00	36.8
4.12	33.6					4.18	33.5	4.44	39.6
4.75	36.2					4.57	35.1	5.00	43.0
5.10	38.2					5.04	37.8	5.49	45.9
5.81	41.7					5.76	40.0	5.67	45.5
6.22	43.9					6.13	41.8	6.00	47.8
6.89	46.9					6.63	42.8	6.18	47.3
7.57	50.2							6.67	54.0
								7.00	51.3

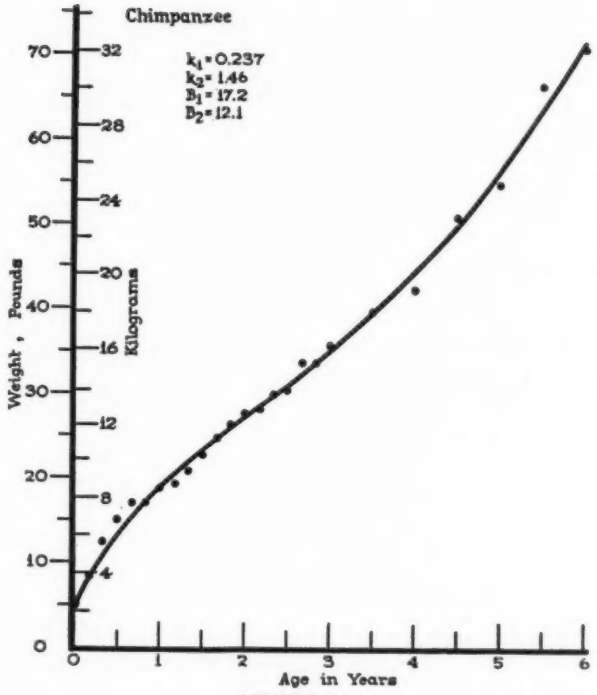

FIGURE 6

FIT OF EQUATION 8 TO THE ORIGINAL DATA ON THE GROWTH IN BODY WEIGHT OF THE CHIMPANZEE, ALPHA, TAKEN FROM SPENCE AND YERKES (1)

represents the ratio of the rate of growth to the "effective weight" for growth,

$$k = \frac{\frac{dw}{dt}}{w'} \tag{9}$$

For the case when $w' = w$, k measures the rapidity of growth from zero, and 100 k is the rate of growth as a percentage of the weight w.

For the case when $w' = A + w$, k measures the rapidity of growth from the quantity A, and 100 k is the rate of growth as a percentage of $A + w$.

For the case when $w' = A - w$, k measures the rapidity of approach to the quantity A and 100 k is the rate of growth as a percentage of $A - w$.

For all cases, 100 k is the rate of growth as a percentage of the "effective weight" for growth.

k is also the "acceleration constant" of growth, and in the extended line of thought presented here takes on a more definite meaning. Taking the second derivative of the weight with respect to time, from the general equation $\frac{dw}{dt} = kw'$

$$\frac{d^2w}{dt^2} = k\frac{dw'}{dt}$$

but

$$\frac{dw'}{dt} = \pm\frac{dw}{dt}$$

for the entire age range, from conception to maturity, so that

$$\frac{d^2w}{dt^2} = \pm k\frac{dw}{dt}$$

and

$$k = \pm\frac{\frac{d^2w}{dt^2}}{\frac{dw}{dt}} \tag{10}$$

where $\frac{d^2w}{dt^2}$ is the acceleration of growth and $\frac{dw}{dt}$ is the velocity of growth. Then k, now called the "acceleration constant," gives the ratio of the acceleration of growth to the velocity of growth, and for any phase of the growth curve, measures the acceleration as a fraction of the velocity, or 100 k is the acceleration of growth as a percentage of the velocity of growth.

In Equation 8, k_1 is the "acceleration constant" for the self-accelerating type of growth and k_2 is the "acceleration constant" for the self-inhibiting type of growth. Also, k_2 measures the rapidity of approach of the self-inhibiting tissues to a constant value, A_2, but in addition, it measures the rapidity of approach of growth to a constant fractional acceleration. If we determine the rate of growth as a fraction of the weight (gain per unit of weight) we have from Equation 8,

$$\frac{\frac{dw}{dt}}{w} = \frac{k_1B_1e^{k_1t} + k_2B_2e^{-k_2t}}{B_1e^{k_1t} - B_2e^{-k_2t}} \tag{11}$$

which on simplification becomes,

$$\frac{\frac{dw}{dt}}{w} = k_1 + (k_1 + k_2)\left[\frac{B_2}{B_1}e^{-(k_1+k_2)t} + \frac{B_2^2}{B_1^2}e^{-2(k_1+k_2)t} + \ldots\right] \quad (12)$$

Since k_1 is small compared to k_2 (k_1 is about one-tenth k_2), k_2 measures the rapidity of approach to k_1, for as t becomes larger $\frac{\frac{dw}{dt}}{w}$ approaches k_1. Figure 7 is a plot of the percentage growth, $100\,\frac{\frac{dw}{dt}}{w}$ versus the age, t, using the values of the constants as determined for the average data of both sexes combined.

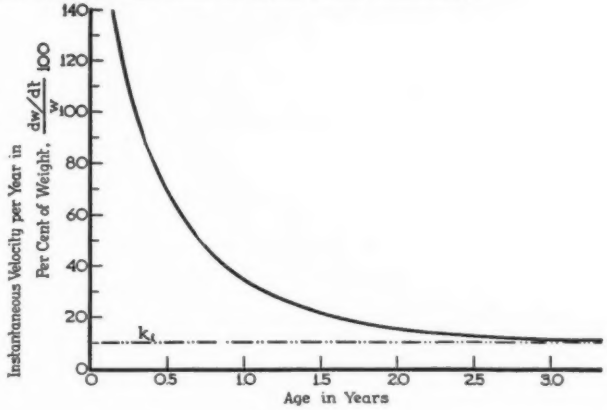

FIGURE 7

PLOT OF INSTANTANEOUS VELOCITY OF GROWTH IN PER CENT OF WEIGHT $\frac{\frac{dw}{dt}}{w}100$, VERSUS AGE

The curve is shown only to about three years of life since from this point to about 14 years the curve is flat at the level of k_1.

F. THE MEANING OF B_1, B_2, A_1, A_2 OF EQUATION 8

Figure 8 is a diagram of the growth curve in body weight from birth to puberty showing the two curves, as dashed lines, of the self-accelerating and self-inhibiting tissues whose sum equals the growth curve. These two curves cannot be explicitly determined, for a

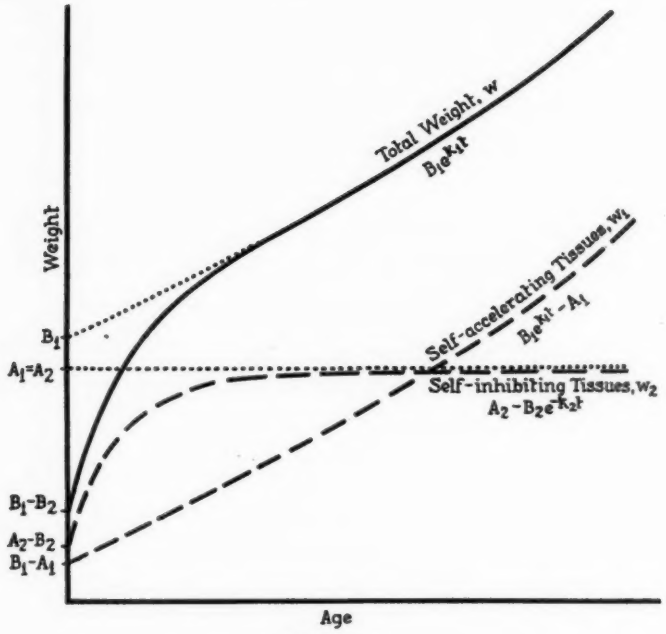

FIGURE 8

DIAGRAMMATIC PLOT OF THE GROWTH CURVE IN BODY WEIGHT FROM BIRTH TO PUBERTY SHOWING THE CURVE OF WEIGHT VERSUS AGE AS A HEAVY LINE AND THE CURVES OF THE SELF-ACCELERATING AND SELF-INHIBITING TISSUES WHOSE SUM GIVES THE WEIGHT CURVE AS DASHED LINES

The constants of Equation 8 are indicated on the chart.

knowledge of w will yield an infinite number of solutions of w_1 and w_2. Figure 8 is merely diagrammatic to show the relations between the constants.

When t is zero, we have $w = B_1 - B_2$ which is the smoothed birth weight. $A_2 - B_2$ represents the birth weight of the self-inhibiting tissues and $B_1 - A_1$ represents the birth weight of the self-accelerating tissues. A_2 represents the weight towards which the self-inhibiting tissues are striving, and A_1 represents the weight-equivalent of the "impulse to grow" of the self-accelerating tissues.

G. SOME APPLICATIONS OF EQUATION 8

The instantaneous velocity of growth in weight per unit time may be obtained by taking the derivative of Equation 8.

$$\frac{dw}{dt} = k_1 B_1 e^{k_1 t} + k_2 B_2 e^{-k_2 t}$$

The instantaneous velocity of growth in pounds per month versus age and versus weight are shown plotted in Figures 9a and 9b. These curves are based on the equation

$$w = 22.11e^{0.0997t} - 13.27e^{-1.2686t} \text{ pounds} \qquad (13)$$

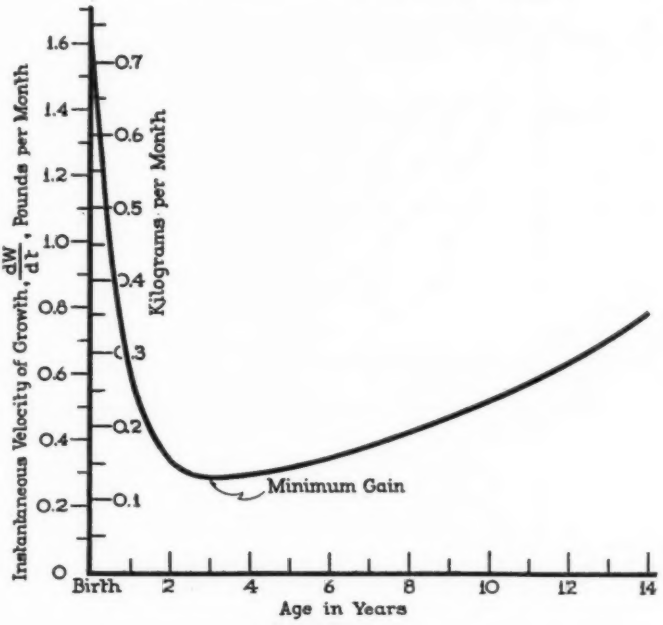

FIGURE 9a

PLOT OF THE INSTANTANEOUS VELOCITY OF GROWTH IN POUNDS PER MONTH VERSUS AGE (UPPER CURVE) AND VERSUS WEIGHT (LOWER CURVE) FOR THE AVERAGE DATA OF WHITE MALES AND FEMALES

The curves are based on Equation 13 as obtained from the data of Table 1. Note that the age when minimum gain may be expected is about three years, and the weight when minimum gain may be expected is about 30 pounds.

with age in years, as fitted to the average growth data for man, both sexes combined.

The age at which the *minimum* gain in weight may be expected is obtained by taking the second derivative of Equation 8, equating to zero and solving for the age.

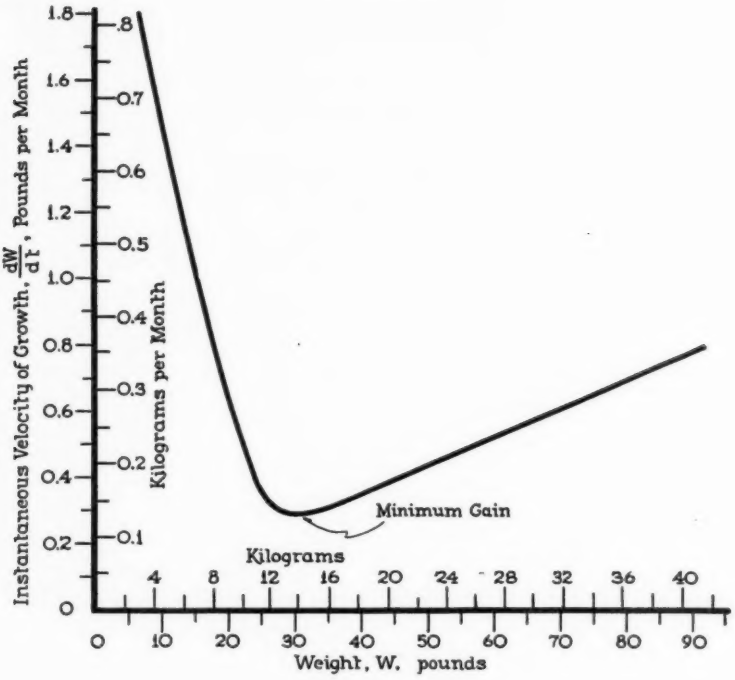

FIGURE 9b

$$\frac{d^2w}{dt^2} = k_1^2 B_1 e^{k_1 t} - k_2^2 B_2 e^{-k_2 t} = 0$$

$$k_1^2 B_1 e^{k_1 t} = k_2^2 B_2 e^{-k_2 t}$$

Taking logarithms and solving for t gives

$$t = \frac{1}{k_1 + k_2} ln \frac{B_2 k_2^2}{B_1 k_1^2}$$

Substituting the constants of Equation 14 gives 3.3 years as the average age when the minimum gain in weight may be expected. The age range when the expected gain in weight is only 0.3 pounds per month or less was calculated to be 2.3 to 4.9 years.

Figure 10 is a plot of man and chimpanzee made somewhat as the equivalence-of-age method with the data for both shown on one curve and with two age and weight axes.

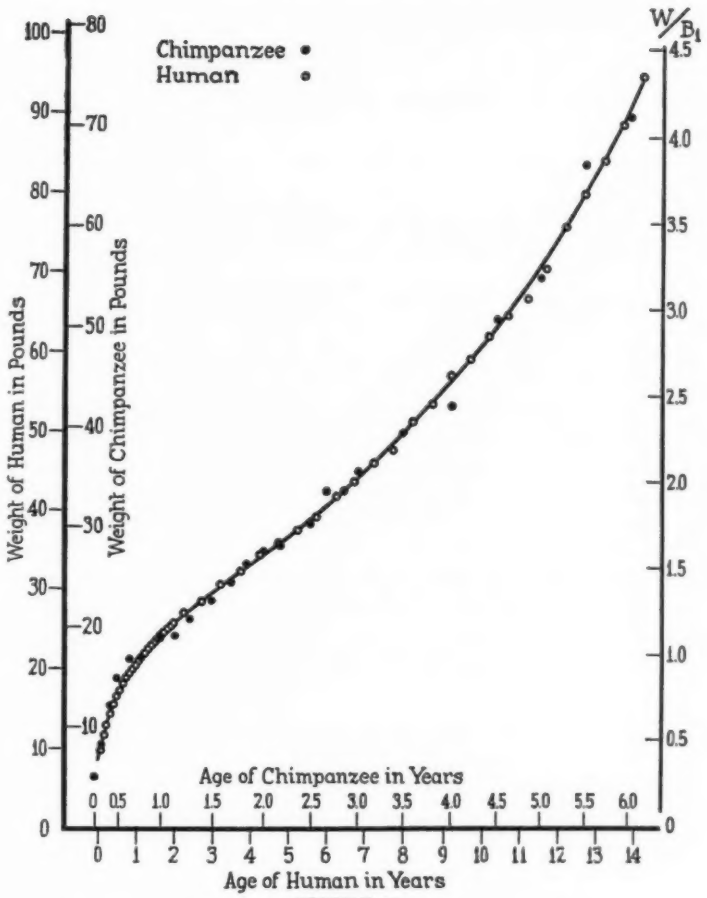

FIGURE 10

PLOT OF THE AVERAGE DATA FOR MAN, BOTH SEXES COMBINED, AND THE DATA OF ONE CHIMPANZEE (ALPHA) MADE SOMEWHAT AS THE EQUIVALENCE-OF-AGE METHOD WITH THE DATA FOR BOTH SHOWN ON ONE CURVE AND WITH TWO AGE AND WEIGHT AXES

From Equation 8 $\frac{w}{B_1}$ was plotted against age for man, the age-scale of the chimpanzee was laid off to correspond to the $\frac{w}{B_1}$ scale, then the appropriate weight scales were laid off.

H. Recapitulation and Summary

The growth in body weight from conception to maturity may be symbolically represented by differential equations of a fundamental kind

$$\frac{dw}{dt} = kw'$$

where w', termed the "effective weight" for growth, must be interpreted according to the various phases of the growth curve, as follows:

	Effective Weight	*Differential Equation*
Prenatal and self-accelerating portion of birth to puberty	$w' = A + w$	$\frac{dw}{dt} = k\,(A + w)$
Self-inhibiting portion of birth to puberty and puberty to maturity	$w' = A - w$	$\frac{dw}{dt} = k\,(A - w)$

For the prenatal phase and the self-accelerating portion of the phase from birth to puberty, the constant, A, indicates an additional factor for growth—a weight-equivalent of an "impulse to grow." For the self-inhibiting portion of the phase from birth to puberty and for the phase from puberty to maturity, the constant, A, represents the limiting amount of growth.

The differential equation representing the rate of growth in body weight from conception to maturity yields the following equations (having different constants) for the various phases of growth:

(a) Conception to 3 months (10 gm. embryo):

$$w = Be^{kt} \qquad \text{(no data shown in this paper)}$$

(b) 3 months (10 gm. embryo) to birth, prenatal:

$$w = Be^{kt} - A$$

(c) Birth to puberty

$$w = B_1e^{k_1t} - B_2e^{-k_2t}$$

(d) Puberty to maturity:

$$w = A - Be^{-kt} \qquad \text{(no data shown in this paper)}$$

The three phases of man's growth in weight prenatal, birth to puberty, and puberty to maturity are represented, respectively, by self-accelerating growth, a combination of self-accelerating and self-inhibiting growth, and finally by self-inhibiting growth.

In addition to fitting the average growth curves for males and females from birth to puberty, 26 individual growth curves are presented. Six have data from birth to about puberty and 20 have data from birth to about six years.

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A REVIEW OF THE APPLICATIONS OF RADIOACTIVE ISOTOPES TO THE STUDY OF GROWTH*

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The purpose of this review is to call attention to the technics which are available through the use of radioactive isotopes for elucidation of the changes in living organisms characterized in the physiological sense as growth changes. Not included in this survey are studies dealing with three types of closely related phenomena: (*a*) simple distribution studies in growing organisms whereby no effect of growth changes is evidenced, (*b*) metabolic studies of young organisms whereby processes are examined which are fundamental to growth but not essentially different from those in adult life, and (*c*) studies of senescence and death of organisms or studies of chromosome destruction whereby no additional light on growth is obtained. In many cases, the data discussed below are taken from large projects in which the primary interest has been to determine (*a*) the distribution rate of some element or compound and (*b*) the amount which reaches a given tissue and is held there at specified times following administration. In these cases only the growth aspect of the data is presented.

Two principal methods of radioactive isotope administration have been used in testing the properties of growth. The simplest is the single dose at time zero after which, at suitable intervals, tissues or compounds are investigated for the extent of the incorporation of the isotope. Studies in which this technic has been employed are presented in the first part of this review. The other method is the repeated administration of the radioactive isotope throughout the course of the experiment with the object of permitting the growth processes to occur in a medium of constant isotope concentration. An alternate and comparable procedure involves the administration of single doses at various times in the life cycle of an organism with examinations at a

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given interval of time after each dose. This procedure also tends to give data from organisms under comparable isotope concentrations. Results from these procedures are presented in the second part of this review.

A. Findings Following a Single Administration of a Radioactive Isotope

1. *Cell Growth*

a. Tissue culture. Brues (1940) has developed a technic for the measurement of the uptake of radioactive substances by cultures of cells. The radioactivity of the cells grown on a thin coverslip attached to one side of a roller bottle can be measured independently of that of the perfusing medium, without removing the cells from their environment. Accumulation of P^{32} (the radioactive isotope of phosphorus) to a higher concentration than that in the extracellular medium has been noted for certain embryonic and adult tissue cells and tumor cells. Not only did growing cells take up the radioactive isotope in significantly higher amounts than surviving cells, but tissue death was followed by release of P^{32} into the surrounding medium. Thus the behavior of cells toward the radioactive phosphorus could be used as an indicator of their viability.

b. Leucocytes and lymphatic tissues. Lawrence and coworkers (1939, 1940) have used P^{32} to study the phosphorus metabolism in leukemia. The absorption and retention of P^{32} were markedly increased in the spleen and lymph nodes and only slightly increased in bone and liver of mice which had been injected with leukemic cells or with lymphoma. While all of these tissues were found to be infiltrated with leukemic cells they showed little if any difference from the normal in total phosphorus content. Thus, the greater uptake and exchange of phosphorus in leukemic tissue would be due to the rapid building of new tissue and its greater rate of metabolism. The nucleoprotein and acid soluble fractions of mouse liver, spleen, and lymph nodes in leukemic infiltration showed a marked increase in the uptake and retention of P^{32}, sufficient to account for the greater rate of phosphorus metabolism of leukemic tissue (Tuttle, Erf, and Lawrence, 1941). Indicative of the rôle of phosphorus in the rapid formation of new tissue is the fact that the white cells of two patients with chronic myelogenous leukemia who had been given P^{32} (Tuttle, Scott, and Lawrence, 1939) showed a rapid initial uptake followed by a

slower rise over a period of days, then a gradual falling off. From 26 to 33 per cent of the white cells consisted of young forms. The use of the isotope has established the importance of the nucleoproteins in leucocyte growth.

c. Cell nuclei. Marshak (1940) determined the activity of nuclei isolated from lymphoma and liver tissue of mice which had received intravenously disodium hydrogen phosphate solution containing P^{32}. The activity per cubic centimeter of packed nuclei as a fraction of the activity per gram of wet tissue was found to remain constantly at 0.3-0.4 for liver up to five days after injection; that for tumor increased to slightly more than 2.0 in the same length of time. Similar results were obtained for Sarcoma 180 in the mouse. *In vitro* experiments showed that the uptake of P^{32} was not due to simple chemical exchange. The data indicate either that the P^{32} may be built into the nucleoprotein directly from the inorganic phosphate or that the rate of turnover in the more labile forms of organic phosphate is very rapid. Since the uptake of P^{32} by tumor nuclei is comparable to that for nuclei from liver which is regenerating after partial hepatectomy, the greater uptake of P^{32} by tumor nuclei as compared with that of normal liver nuclei can be attributed to mitotic activity.

From data for the nuclear P composition of liver and of tumor, and from the nuclear P^{32} content at 48 hours, the specific activity of tumor nuclei has been found to be more than four times that of liver nuclei. From the daily P^{31} retention and the percentage of P^{32} uptake, Marshak calculated that each nucleus would incorporate a quantity of P^{31} equal to 8.9 per cent of its total P^{31} content in five hours, thus taking 56 hours to introduce into the nucleus the quantity of P^{31} equal to that it originally contained. This value is the time required to synthesize a new nucleus and agrees approximately with the observed rate of growth of the tumor.

d. Seeds. Hevesy, Linderstrøm-Lang, and Olsen (1937) germinated maize and pea seeds until the rootlets were 2-3 cms. in length and then transferred them to solutions containing P^{32}. A marked difference in the distribution of P^{32} was found when the various parts of the maize plants were compared with analogous parts of the pea plants. In the maize, the germ contained P^{32}, the endosperm did not. In the pea, the rootlet and leaf and also the cotyledon contained P^{32}; however the rootlet and leaf were richer in P^{32} than the cotyledon. These facts reflect the fundamental differences in the growth processes of these two types of seeds.

2. *Phospholipid Metabolism*

a. Chick embryo. Hevesy, Levi, and Rebbe (1938) were interested in determining whether the developing chick embryo made use of the large store of phospholipids present in the yolk or whether it synthesized these compounds from inorganic phosphorus. Injection of radioactive sodium phosphate into hen eggs was followed by incubation for periods of 6, 11, 16, and 18 days. At all these incubation times the phospholipids from the yolk were only slightly active while those from the embryo were strongly active; thus the phospholipid molecules of the embryo were not taken directly from the yolk but were synthesized in the embryo. On the other hand, the inorganic phosphorus present in the embryo was taken as such from the yolk or the white. However, practically all the organically bound phosphorus atoms in the yolk which eventually appeared in the embryo have passed through the stage of inorganic phosphorus before incorporation into the various compounds of the embryo. The use of radioactive isotopes has shown that in mobilizing the reserve foods of the yolk a degradation to simpler forms is an essential part of the growth process.

b. Tumors. Jones, Chaikoff, and Lawrence (1939, 1940) used P^{32} to determine the rate of phospholipid turnover during the growth of four transplantable mouse tumors: a mammary carcinoma, a lymphoma, a lymphosarcoma, and Sarcoma 180. They concluded that the phospholipid metabolism of these tumors resembled that of liver and intestine rather than that of muscle and brain. However, the phospholipid activity, i.e., the percentage of the administered labelled phosphorus in the phospholipid per gram of tissue, was not uniform in the four types of tumors investigated. Since the phospholipid activities of mammary carcinoma and of lymphoma were very similar and twice as great as those of Sarcoma 180 and of lymphoma, cell type does not seem to determine the extent of such activity. Thus, it would appear either that each tumor may have a characteristic phospholipid metabolism, or that the phospholipid activity of a tumor may be the result of effects produced upon the host by the tumor itself. In order to settle this point, two different types of tumor were inoculated into the same animal. At intervals of from 11 to 21 days after inoculation, P^{32} was administered and the tumors removed at varying times thereafter. Since each type of tumor was found to maintain its characteristic phospholipid activity, such activities must be independent of the metab-

olism of the host. Furthermore, a comparison of the growth curves for the different tumor types with their respective phospholipid activities revealed that the latter are also independent of the tumor growth rates.

Kohman and Rusch (1941), comparing the turnover of P^{32} of tumorous liver cells resulting from administration of dimethylaminoazobenzene with that of normal liver cells, found the nucleoprotein metabolism of the tumorous cells significantly increased over that of the normal cells.

Thus, the use of radioactive isotopes has provided a basis for the classification of certain tumors into types based on the characteristic phosphorus metabolism which in each case is a property of the tumor independent of its cell type, growth rate, or the effect of the host on the tumor.

3. *Bone and Tooth Substance*

a. Growth of bone. Skeletal growth has been studied in young adult rats using P^{32} (Manly and Bale, 1939). In the 20 days following the administration of a single dose, three significant findings were observed: (*a*) the blood P^{32} to P^{31} ratio rose at first and later fell, (*b*) the bone ratio rose and remained nearly constant so that (*c*) finally the bone ratio was greater than that of the blood. To explain these observations, Manly, Hodge, and Manly (1940) assumed (*a*) that a portion of the bone was in continuous equilibrium with the blood phosphorus (labile bone) but the remainder was not (stable bone), and (*b*) that the accretion rate of bone was constant but the newly deposited calcific material had the P^{32} to P^{31} ratio currently in the blood. Based on the P^{32} to P^{31} ratio for diaphyseal bone, it was shown that the increase of P^{32} which was due to new calcification demanded an increment of about 1/50th of the skeleton per day; this would involve a deposition of the order of 10 mg. of phosphorus per day. The data from Donaldson (1924) on the rate of skeletal growth in rats of the same age checked this figure exactly. Evidence of the skeletal growth rate may also be seen in the partition of P^{32} between labile and stable bone at various times after administration. For example, in the epiphyseal bone in 24 hours 95 per cent of the P^{32} was in the labile, 5 per cent in the stable portion; on the 20th day, 21 per cent was in the labile, 79 per cent in the stable portion. This indicated a high growth rate in epiphyseal bone; in fact it was found to be higher than in diaphyseal bone.

b. Growth of incisors. Manly and Bale (1939) also found that 24 hours after a single dose of P^{32}, 73 per cent of the P^{32} found in the rat incisor was present in the labile portion, 27 per cent in the stable; on the 20th day these values were respectively 3 and 97 per cent. The growth (accretion) rate of the incisor was about three times that of diaphyseal bone. Extrusive growth of the incisors was shown by the changes in the P^{32} distribution between root, middle, and tip thirds of the incisor during the 20-day period. Thus, after one day, the P^{32} percentages in these three portions were 76 : 21 : 3, respectively, and, after 20 days, 46 : 40 : 15, respectively. The amount of P^{32} increased in the middle and tip thirds during the 20 days showing the extrusive growth, but in the roots the P^{32} increased only until the 13th day after which it fell. Five days after the dose, the blood P^{32} level was falling rapidly; however, the incisor P^{32} values steadily increased. Perhaps the P^{32} stored in the rest of the skeleton was being drawn on by the blood to furnish P^{32} for root calcification.

c. Growth of molars. Molars in the rat (Manly and Bale, 1939) gave evidence of a low accretion rate, as would be expected. Volker (personal communication) has shown that the persistently growing guinea pig molars pick up higher proportions of a single dose of P^{32} than the permanent rat molars do. Sognnaes and Volker (1941) have also shown that the unerupted third molars of a monkey are still growing (calcifying); the enamel and dentine of such teeth have a remarkable ability to fix P^{32}, numerically almost equal to that of jaw or long bones. The radioactive isotopes have shown the differences in inorganic metabolism of permanent teeth at different developmental stages.

d. Rickets. The healing of rickets may not be a normal growth process, but studies of this sort of bone growth have given some evidence of the role of Vitamin D in calcification. Dols et al. (1938, 1939) have shown that one day after a single dose of P^{32} less of the isotope was found in the skeletons of normal than in those of rachitic chickens. However, Morgareidge and Manly (1939) have shown that rachitic and normal rats had comparable blood P^{32} levels over a 3-day period and the same bone P^{32} levels for 72 hours whether they received Vitamin D (orally) or not. It was not until 72 hours after Vitamin D treatment that rachitic rats showed an increase in the bone P^{32} with a simultaneously appearing positive line test. This evidence combined with that of Cohn and Greenberg (1939) indicated that Vitamin D is concerned in the growth of bone.

B. Findings Following Repeated Administrations of a Radioactive Isotope

There are two ways in which the technic of repeated doses may be applied to studies of growth changes: (*a*) repeated doses to one animal are followed by repeated samples of the same tissue (blood, urine, muscle), and (*b*) repeated doses are used with a number of animals, each of which is sacrificed at a different time after the initiation of the experiment. Both of these procedures have the same advantage, namely, that the changes observed have taken place with the environment (internal or external) at a constant isotope concentration. A third method, which achieves this constancy but is a repeated administration only metaphorically, consists of selecting a number of animals differing in age or in the developmental stage of a certain tissue and administering to each a single isotope dose, then sacrificing each animal at the same time interval after administration. Since the isotope concentration in an organism usually rises rapidly immediately after administration, goes through a maximum, and then falls, this procedure provides for the examination of tissues at comparable isotope concentrations. Each of these three methods has been employed in isotope studies, but so far examples of only the latter two have given information on growth processes.

1. *Brain*

In 1938, Changus, Chaikoff, and Ruben, using P^{32}, found a very low rate of phospholipid turnover in rat brain. However, they observed that in younger animals greater amounts of P^{32} were incorporated into the brain phospholipid than in older animals. This variation in phospholipid activity with age was studied by Fries, Changus, and Chaikoff (1940) in the forebrain, cerebellum, medulla, and cord of rats of body weight 5-6, 15, 25, 30, 50, 100, 200, and 300 grams. In all parts of the central nervous system the highest phospholipid activity was found on the day of birth. The phospholipid activity then declined greatly until the rat attained a weight of 50 grams. Between body weights of 30 and 50 grams, an abrupt change in phospholipid activity of all parts of the central nervous system occurred. With growth beyond 50 grams, phospholipid activity decreased throughout the central nervous system but at a much slower rate than that between birth and 50 grams. The phospholipid activity of the cord decreased more rapidly than that of the medulla, forebrain, and cere-

bellum. The use of P^{32} has shown the relation of the phospholipid activity with the morphology of the brain.

2. *Placenta*

Flexner and Pohl (1940), using Na^{24} in pregnant cats, have studied the growth changes in the transfer of sodium from the maternal circulation to that of the fetus. The younger the fetus, the more rapidly the transfer per unit weight of fetus occurred. This phenomenon apparently depended on the relative growth rates of placenta and fetus; the placenta weighs about 50 times as much as the fetus at 15-20 days but only 1/5 as much at term. Changes in the placenta also occur; on a weight basis, the earlier placenta transferred sodium more slowly. These workers have further established that the changes in rate of fetal growth are accompanied by parallel changes in rates of placental transfer of sodium, the latter rates calculated per gram of fetus.

3. *Incisors*

Repeated doses of P^{32} were used by Hevesy, Levi, and Rebbe (1940) to study the growth of rabbit incisors. The root portion of the incisor dentine in 50 days had the same P^{32} content as the plasma, the middle and tip portions 99 and 44 per cent, respectively, as much. Incisor enamel in the root and middle portions had 82 per cent of the plasma P^{32} content, while the tip portion had 7 per cent. Thus, using the repeated dose technic, the effect of extrusive growth is also demonstrated by the high values of P^{32} in the middle and tip portions of the incisor.

C. Discussion

The primary aim of this review has been to present the usefulness of radioactive isotopes as tools in the study of growth processes. Consequently, the two technics which have so far given information about these processes have been stressed by dividing the review into two parts: (*a*) findings following a single administration of a radioactive isotope, and (*b*) findings following repeated administrations. However, to gain insight into the sorts of information on growth which can be obtained, the studies with radioactive isotopes may be classified roughly into several categories.

1. The time in the growth cycle when certain compounds appear. Examples: Marshak's work on nucleoproteins, Hevesy's work on eggs.

2. The time when morphological or histological differentiation occurs. Example: Morgareidge and Manly, effect of Vitamin D in rickets.

3. The rate at which a given compound appears. Example: Manly on bone calcification rates.

4. The rate at which a certain tissue grows. Examples: Lawrence on leukemia, Jones on tumor, Hevesy on incisors.

5. The differences in growth processes in different organisms. Example: Hevesy on maize vs. pea.

6. The differences in distribution rates and amounts in young as compared with adult tissues. Examples: Changus on brain, Flexner on placenta.

The meagerness of the number of these examples is an excellent illustration of the many opportunities for further work along these and related lines. With the increasing availability of many isotopes (Bale, 1940) and with the realization of their usefulness, it is believed that many workers will employ these tools in the furtherance of their current researches on growth.

D. Summary

Radioactive isotopes may be used in the study of growth phenomena either by a single administration or by repeated administrations with examinations of tissues at suitable intervals. In the former method, the isotope concentration in the body is continuously variable with time; in the latter method, the isotope concentration is maintained as nearly constant as possible.

Although few investigations have been reported, to date, in which the sole object has been the study of growth, many investigations have contained some data pertinent to the subject. These data, in many cases fragmentary, have been reviewed.

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A SIMPLIFIED METHOD FOR COMPUTING THE THEORETICAL CLASS FREQUENCIES OF A BINOMIAL EXPANSION

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Characters, or events, in an experimental series happen with an observed frequency and in an observable pattern. It is thus a matter of common biological necessity to determine the pattern in which an event or character is distributed through an experimental population. There are two reasons for this. First, that a change in the pattern between two experiments indicates a positive result with just as much validity as does a change in the total frequency. Second, that the adequacy of the size of a sample, particularly of a control, can be judged by the "naturalness" of the distribution pattern. "Naturally" occurring events normally follow a known pattern: if the event under investigation in the control series follows such a pattern, then it may be deduced that the control is adequate. Thus in the example discussed below, the close agreement of the pattern of the deaths following injection of normal saline with the binomial pattern known to be followed by natural deaths, demonstrates both the adequacy of the size of the sample and the reliability of normal saline as a control.

The commonest distribution patterns found in biological experiments are the "normal," the "binomial," and the "Poisson." In the relatively small populations usually investigated in biological experiments, Poisson distribution is only found for occurrences of which the probability is less than 0.10; theoretically perfect normal distribution is only found when the probability of occurrence is 0.50; distributions of characters which represent less than 50 per cent and more than 10 per cent of the population should therefore lie on a binomial expansion. It is evident that the binomial distribution most adequately represents the majority of biological observations and should be used as a standard of comparison, and that the generalized

form of this expansion should be used in preference to the specialized cases represented by the "normal" and "Poisson" series. That these general binomial frequencies are not used is due to the inordinate labor of computing them from the formula in established usage, as compared with the simplification given by published tables in the calculation of the special cases. The present paper presents a method of computing general binomial class frequencies with as little trouble as is involved in computing "normal" distributions.

The standard formula for computing the class frequency (f) of an observation (x) in a binomial of total frequency N is:

$$f = N \frac{n(n-1)\ (n-2) \ldots (n-x+1)}{x!} p^x q^{n-x} \qquad (1)$$

or the algebraic equivalent:

$$f = N \frac{n!}{(n-x)!} p^x q^{n-x} \qquad (2)$$

where n is the number of opportunities of occurrence, or the number of objects in each of the groups into which the data is divided: p is the probability of occurrence and q the probability of non-occurrence. p and q are, of course, expressed in decimal fractions of *1* and can therefore vary, within the limits of the expansion under discussion, between 0.10 and 0.90.

Re-writing (2) in logarithmic form:

$$\log f = \log N + \log n! - \log x! - \log (n-x)! + x \log p + (n-x) \log q \qquad (3)$$

Expanding the last two terms and factoring:

$$x \log p + (n-x) \log q = x (\log p - \log q) + n \log q$$

Substituting this expansion for the last two terms of (3) and grouping all functions of x at the right:

$$\log f = \log N + \log n! + n \log q + x (\log p - \log q) - [\log (n-x)! + \log x!] \qquad (4)$$

But N, n, p, and q are constants for any binomial distribution. Functions involving these are therefore constants throughout the whole computation; two such constants may be extracted:

$$\text{let } K = \log N + \log n! + n \log q$$
$$k = \log p - \log q$$

Substituting these values in (3):

$$\log f = K + xk - [\log (n-x)! + \log x!] \qquad (5)$$

TABLE 1

COMPUTATION OF THE BINOMIAL CLASS FREQUENCIES (f_{bin}) BY THE SHORT METHOD DESCRIBED IN THE TEXT

The experiment analyzed, records the number (x) of deaths observed in each of 64 groups of 20 eggs injected with normal saline. The computation of the mean ($M = 3.47$, hence $p = .1735$ and $q = .8265$) is not shown. The comparison of the observed frequencies (f_{obs}) with the calculated binomial frequencies is better seen in Table 2.

x	0	1	2	3	4	5	6	7	8	9
f_{obs}	1	7	12	15	12	9	5	2	0	1
xk	0	9.32206*	8.64412*	7.96618*	7.28824*	6.61030*	5.93236*	5.25422*	4.57648*	3.89854*
$K + xk$	18.53710	17.85916	17.18122	16.50328	15.82534	15.14740	14.46946	13.79132	13.11358	12.23564
$log\ (n - x)!$	18.38612	17.08509	15.80634	14.55107	13.32062	12.11650	10.94041	9.79428	8.68032	7.60116
$log\ x!$	0	0	0.30103	0.77815	1.38021	2.07918	2.85733	3.70243	4.60552	5.55976
	18.38612	17.08509	16.10737	15.32922	14.70083	14.19568	13.79774	13.49871	13.28586	13.16092
$log\ f_{bin}$	0.15098	0.77407	1.07385	1.17406	1.12451	0.95172	0.67172	0.29261	9.82772*	9.07472*
f_{bin}	1.42	5.94	11.85	14.93	13.32	8.95	4.70	1.96	0.67	0.12

$N = 64$
$n = 20$
$p = .1735$
$q = .8265$

$K = log\ N + log\ n! + n\ log\ q$
$= 1.80618 + 18.38612 + 20(9.91724 - 10)$
$= 18.53710$

$k = log\ p - log\ q$
$= 9.23930* - 9.91724*$
$= 9.32206*$

Note: —10 has been omitted after the logarithmic values marked *.

TABLE 2

COMPARISON OF THE OBSERVED FREQUENCIES (f_{obs}) GIVEN IN TABLE 1 WITH THE THEORETICAL NORMAL (f_{norm}), AND THE THEORETICAL BINOMIAL (f_{bin}) FREQUENCIES BY THE χ^2 TEST FOR GOODNESS OF FIT

X	f_{obs}	f_{norm}	$\frac{(f_{norm}-f_{obs})^2}{f_{norm}}$	f_{bin}	$\frac{(f_{bin}-f_{obs})^2}{f_{bin}}$
0	1	2.04	0.45	1.42	0.01
1	7	5.41	0.31	5.94	0.19
2	12	10.23	0.31	11.85	0.00
3	15	14.08	0.06	14.93	0.00
4	12	13.93	0.26	13.32	0.13
5	9	9.91	0.08	8.95	0.00
6	5	5.08	0.01	4.70	0.02
7	2	1.90	0.00	1.96	0.00
8	0	0.51	0.51	0.67	0.67
9	1	0.11	7.71	0.12	6.40
			$\chi^2 = 9.16$		$\chi^2 = 7.42$
			$P = 0.40$		$P = 0.63$

This formula is very simple to use, since tables of the values of *log n!* are now readily available. After the single computations of K and k, it is only necessary to perform one simple multiplication (xk, where x is almost always a low integer), and one addition of logarithms taken directly from a table [*log* $(n - x)!$ and *log* $x!$], to arrive at *log* f by one subtraction.

An example of this operation is given in Table 1. k is first calculated and the line xk entered. K is then computed and $K + xk$ written in. *Log* $x!$ and *log* $(n - x)!$ are entered from the tables and their summation written down as the next line. The subtraction of the values in this line from the values of $(K + xk)$ give the logarithm of the binomial frequency.

The labor of the whole computation compares very favorably, both in simplicity and quantity, with that required to compute the normal distribution. In the latter case it would be necessary first to derive the standard deviation from the summation of the squares of the deviations; then to derive the quotient d/s, and from it the value of the ordinate; then to secure the product of the ordinate with the function y_0. There is no comparison of the labor involved in using the usual formulæ (1 and 2) with that of the simplified formula (5).

In view of the simplified method here given, it is interesting to show a comparison of a normal with a binomial distribution. This is given in Table 2 where it is shown that, for as few as 64 groups, there is a considerable difference in the probabilities of goodness of

fit obtained from the χ^2 test. In larger experiments the divergence is far more striking but even in the example given there is a swing from probability in favor of, to probability against, random distribution. Reverting to the argument of the first paragraph, the comparison with the binomial distribution therefore shows a probability that the sampling and control are adequate; the more commonly employed comparison with normal distribution considerably reduces this probability.

The method described in this paper has another advantage. The values of p and q are mutually dependent; x, in any given set of experiments, does not commonly vary over a wide range. The value of $xk = x\ (log\ p - log\ q)$ can easily be computed over the range likely to be found and the values tabulated in an internal entry table. With such a table the whole of the binomial analysis of a given set of data reduces to a single computation (K). All other values can be entered directly from tables.

It is hoped that the simplified method here presented will lead to a greater use of general binomial frequencies; and a corresponding reduction in the use of the special case of the "normal" curve with its inherent fallacy that all events are equally probable, even those known not to be.

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TRANSPLANTATION EXPERIMENTS WITH AN ECTODERMAL GROWTH OF FROG EMBRYOS[1]

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A. Introduction

From the work of Witschi ('22, '24, '30, '34) it is known that delayed fertilization of frog eggs produces sex reversal and, in embryonic stages, a series of developmental abnormalities including neoplastic growths. The embryonic tumors have been described briefly and some transplantation experiments recorded. According to Witschi ('30) a delay of 3 to 5 days in the uterus before fertilization results in a multiplicity of teratological developments involving "loss of power of differentiation in the embryonic cells and the tendency to start neoplastic growth." The epidermis thickens and often gives rise to a characteristic epithelioma, big tumors appear in the intestinal wall, and mesenchyme cells attack and infiltrate neighboring tissues. Embryos bearing such growths die within two weeks. In an attempt to propagate the growths, transplants were made subcutaneously behind the ear or into the body cavity of tadpoles. Some of these underwent regression while others developed into infiltrating growths. The number of cases is not given. The fate of one infiltrating growth is described. A just metamorphosed frog which had carried a strongly growing implant for 22 days, was found at autopsy to have a heavily infiltrated reticulum which was then transplanted, together with most of the viscera, into the body cavity of an adult frog. Sixty-two days later this animal was found to have a large infiltrating and metastasizing tumor in the body cavity.

The development of tumors in embryos is a subject of considerable interest as pointed out by Needham (1936). There is first the general question of possible effects of morphogenetic fields on the structure and behavior of tumors. Such fields of induction are known to be present in embryos but appear to be absent from adults of most forms

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above Urodele amphibians with the exception of certain reptiles. In the case of the embryonic tumors produced by delayed fertilization there are other suggestive considerations also pointed out by Needham who noted that Witschi's observations might all be interpreted as the result of an upset in sterol metabolism. Thus there could be produced an alteration of sex hormones, uncontrolled liberation of evocator, and production of carcinogenic substances leading respectively to (*a*) sex reversal, (*b*) axial duplication and monster formation, and (*c*) neoplastic growth.

Considerations of this nature suggest that tumors in embryos may be of importance in elucidating some aspects of malignant growth. For further studies it is first necessary to have a readily procurable and genuinely malignant growth. Abnormal growths developing on *Rana pipiens* embryos following delayed fertilization have been examined in some detail to determine if any of them fit these requirements. The results (Briggs, '41) show that only one of these, an ectodermal papilloma,[2] grows progressively on overripe embryos. Hosts bearing it are retarded in growth rate and die within two or three days after the papilloma first appears. The present article reports experiments which were made to determine if this growth would continue to grow progressively when grafted to normal hosts.

B. Materials and Methods

The *Rana pipiens* used in this study were collected in the vicinity of Montreal. Witschi used the European species, *Rana temporaria*, and the material we have used is accordingly not identical. Frogs were collected in the late fall and kept in slowly running tap water at about 3° C during the winter. Most of the experiments were performed between December and April. Overripe eggs were obtained as follows: A female, brought first to room temperature, was injected with 1 or 2 *R. pipiens* pituitaries macerated in 1cc distilled water. Within 18 to 24 hours the ovaries had ovulated and the eggs were in the uterus. About 300 eggs were stripped into a sperm suspension on each of the successive five days. These were distributed 50 per finger bowl containing 80 to 100cc of 10 per cent Ringer's. Embryos were reared for one day in 10 per cent Ringer, and subsequently in boiled tap water at about 20°-22° C.

[2]This growth is made up of folds and papillae composed entirely of ectodermal cells. As a matter of convenience it will be referred to as a papilloma in the present report although it lacks the stroma characteristic of mammalial papillomas.

Abnormal growths appeared in most instances where there had been a post-ovulatory delay in the uterus of three to five days. These have been described in detail elsewhere (Briggs, '41). Three of the four types commonly observed are undoubtedly benign. The fourth is a non-vesiculated papilloma-like ectodermal growth 6 to 10 cells thick, appearing first on 4mm to 8mm embryos. In 15 per cent of the observed cases it spread progressively over the surface of the host. The growth of the host was retarded and death ensued about three days after the first appearance of the growth. Grafts were made of progressively growing papillomas to the following sites in normal animals: (*a*) the anterior chamber of the adult eye (67 cases), (*b*) subcutaneously to tadpoles (102 cases), and (*c*) to the flank and body cavity of embryos of an age approximately the same as that of the "overripe" donors (216 cases). The subcutaneous and eye implants were made by slitting the skin or cornea with a small corneal knife. A piece of papilloma tissue was introduced through the slit with fine forceps or was injected with a specially constructed glass hypodermic needle. The tissue was manipulated after introduction with a small glass rod. The same technique was used in making the body cavity implants to 8mm-9mm embryos (Stages 21-22 of Pollister and Moore, '37).

The majority of grafts to embryos were made to the flank of hosts at Stage 17-18 (tail bud). A circular piece of ectoderm plus underlying mesoderm was carved from the right flank of the host with fine iridectomy scissors. A piece of papilloma tissue was similarly prepared and quickly pushed into place with a blunt glass rod, then held in position with a glass clamp for 15 to 30 minutes. Due to the irregular form and strong ciliary activity of the tissue 40 to 50 per cent of the grafts failed to heal properly and were lost within a few hours. In an attempt to obtain a larger percentage of "takes," a small piece of papilloma tissue was placed beneath a normal graft of flank ectoderm plus mesoderm in 16 homoplastic and 38 heteroplastic cases. The papilloma tissue worked its way to the surface and healed in between the adjacent edges of graft and wound in 60 per cent of the cases. In the remainder the implant was lost. Results from the two types of operation are identical and are therefore described together in the next section of the paper. A part of the overripe donor was preserved at the time of the operation. Hosts were observed closely and preserved at daily intervals from one to seven days after operation. Observations were continued for 15 to 30 days and tadpoles preserved

at irregular intervals during later development. The histological procedure was the same as that described in the previous paper (Briggs, '41). Operations were performed in Holtfreter's solution sterilized by boiling before addition of $NaHCO_3$ which was rendered as sterile as possible by repeated freezings in dry ice. Glassware and instruments were flamed or rinsed with 95 per cent alcohol. The hosts were left in Holtfreter's solution for one day after operation, then were returned to tap water rendered sterile and chlorine-free by boiling. Temperature conditions:—Hosts were kept before operation at temperatures ranging from 12° to 22° C in order to control developmental rate so that they would be at the proper stage when needed. Donors were reared at 12° to 15° and at 20° to 22° C. Operations were performed and hosts reared after operation at room temperature (20°-22° C).

C. Results

1. *Papilloma Grafts to Similar Age Host Embryos*

a. Heteroplastic grafts of Rana pipiens papilloma tissue to the flank of normal Rana palustris hosts. Table 1 summarizes the results

TABLE 1

Behavior of *Rana Pipiens* Ectodermal Papilloma from "Overripe" Donors Grafted to Normal Hosts of Approximately the Same Age

All heteroplastic grafts made to the right flank of *R. palustris* tail bud hosts (st. 17-18). Three of these hosts developed papillomas made up of host tissue. Homoplastic grafts made to the right flank of st. 17-18 and to the body cavity of st. 21-22. Homoplastic control grafts—flank ectoderm plus mesoderm from normal controls for overripe donors grafted to right flank of normal hosts at st. 17-18. The five cases of abnormal post-operational development were all oedematous tadpoles. Post-operational deaths were all due to failure of the wound to heal.

Type of graft	No. of donors	No. of grafts (1 per host)	No. of "takes"	No. of hosts developing papillomas	No. of hosts in which grafted papilloma incorporated as normal ectoderm	Abnormal post-operational development	Post-operational deaths
Heteroplastic	24	143	87	3 (host tissue)	84	2	8
Homoplastic	12	63 (St. 17-18)	38	6	32	3	2
		10 (St. 21-22)	10	0	—	0	0
Homoplastic controls	10	59	53	0	—	0	0

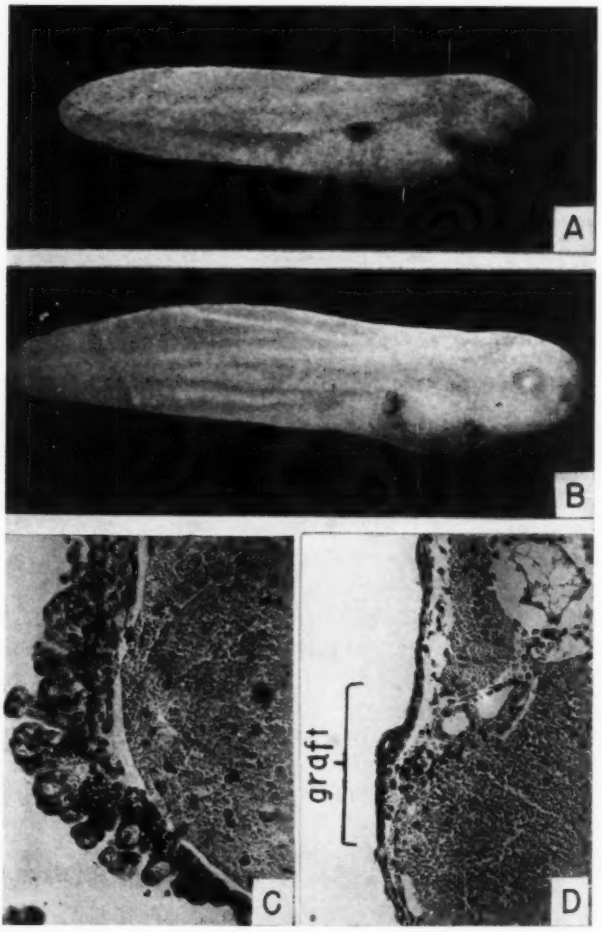

FIGURE 1

A—*Rana palustris* host embryo two days after receiving a flank graft of *Rana pipiens* ectodermal papilloma tissue. 12.3 x.

B—*Rana palustris* host four days after receiving a flank graft of *Rana pipiens* papilloma. The darkly pigmented graft cells are incorporated as normal ectoderm and dispersed over a wider area. 12.3 x.

C—Cross section of an "overripe" *R. pipiens* donor embryo showing ectodermal papilloma. 96 x.

D—Cross section of a *Rana palustris* host two days after operation. The darkly pigmented grafts of *R. pipiens* papilloma tissue is smoothly incorporated; it retains only an indication of one of its papillae. 104 x.

of these experiments. Out of 87 successful grafts there were no cases of continued progressive growth of the papilloma on normal *palustris* hosts. During the first day after the operation the densely pigmented *pipiens* tissue is very distinct on the light *palustris* host. At first the folds and papillae of the papilloma are maintained in the new site, but on the second and third days they become smooth and flat (Figure 1A). With continued growth of the host the *pipiens* cells are gradually moved from their original site. Thus the graft becomes diffuse, and is perfectly incorporated into the host ectoderm (Figure 1B). As a result of two factors—the dispersion of the graft cells and a decrease in the amount of the primary pigmentation per unit area—it becomes impossible in most cases to locate definitely the *pipiens* tissue during tadpole stages. However, 34 tadpoles were observed carefully for approximately 15 days. These were dissected at the end of this period (14mm to 17mm stages) and were found to be perfectly normal with no sign of a growth at the graft site. An additional 36 tadpoles were similarly observed for approximately 30 days (20mm to 25mm stages) and were also found to be perfectly normal.

A total of 35 hosts taken on the second to sixth days after operation have been examined in serial sections. Twelve donors have been similarly examined. Figure 1C shows a typical papilloma used in these experiments. Cells making up this growth have already been described in another paper (Briggs, '41) as having the same components and staining properties as normal cells while differing as to size and shape and arrangement of cells; and in a minor way in the arrangement of cell components. Apparently these points of difference are not of unalterable character for grafted papilloma tissue is seen in sections to become perfectly incorporated into the host ectoderm. For the first two or three days (host = 6mm to 8mm) the graft cells, as already noted from gross observations, remain localized and easily detectable. The original contour of the papilloma is gradually lost (Figure 1D). By the fifth and sixth days (host = 10mm to 11mm) the graft is more diffuse, and in sections appears as a number of more or less separate groups of darkly pigmented cells. There is now no sign of papilloma-like arrangement of the cells.

In three exceptional cases papilloma-like growths developed on *Rana palustris* hosts which had received grafts of *Rana pipiens* papilloma tissue. Examination of the embryos in toto and in serial section showed these growths to be composed of host tissue. The hosts bearing them were retarded, being 5.5mm, 5.7mm, and 5.8mm in length

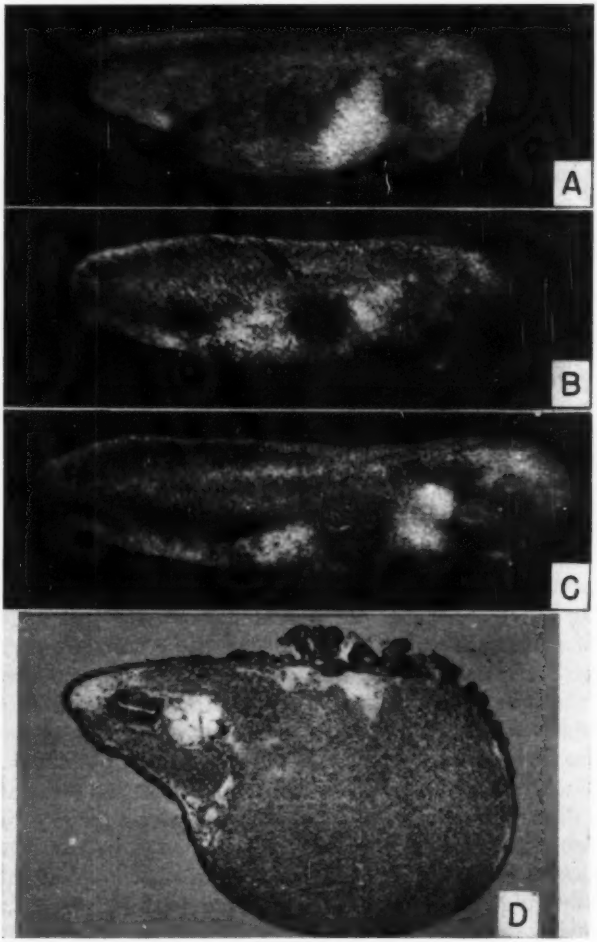

FIGURE 2

A—*Rana pipiens* host 22 hours after receiving a flank graft of *R. pipiens* papilloma tissue. The large circular area on the flank is a graft of normal ectoderm plus mesoderm. At the posterior border of the normal graft is a small, dark, slightly elevated area—the papilloma tissue. 14.5 x.

B—The same host 29 hours after operation. The dark, slightly elevated area has spread to include tissue surrounding the graft site. 14.5 x.

C—The same host 51 hours after operation. The darkly pigmented area visible in *B* has increased in size and is now thrown into folds and papillae. 14.5 x.

D—Cross section of a *Rana pipiens* host 68 hours after receiving a flank graft of *R. pipiens* papilloma tissue from an "overripe" donor. Note the papilloma-like enlargement of the flank ectoderm. The central part of the growth has begun to necrose. 53 x.

(2½ days post-operation), while control embryos were 6.5mm and 7.4mm.

b. Behavior of grafts of Rana pipiens papilloma tissue to the flank of normal Rana pipiens hosts. Table 1 gives a summary of the results. In 32 of the 38 "takes" the behavior of the grafted papilloma was exactly the same as that described for the heteroplastic grafts. During the first day or two following the operation the papilloma tissue remains distinguishable by virtue of its irregular surface. With subsequent development of the host the folds and papillae of the graft become flattened and smoothed out. By the fifth and sixth days it is indistinguishably incorporated into the normal host ectoderm.

Twenty-two of the 38 "takes" were observed carefully for 15 to 30 days during which they developed to stages ranging from 20mm to 32mm. The graft site was examined carefully under a dissecting microscope: no growths or other abnormalities were found.

In six exceptional cases papilloma-like growths developed on normal hosts after they had received grafts of papilloma tissue. Figures 2A, B, and C are a series of photographs of one such host taken at intervals over a 2-day period following the operation. In this particular case the operation was made by placing a small amount of papilloma tissue beneath a graft of normal ectoderm plus mesoderm. Within a few hours after the operation the papilloma tissue had migrated to the surface and was healed in on one side of the normal graft (Figure 2A). In the five additional cases of progressive growth the original graft was made to the surface of the host and healed in completely within approximately three hours. The subsequent behavior of the papilloma tissue followed the same pattern in all six hosts.

At 12 hours, 24 hours, and 36 hours after operation the graft tissue remains discernable but no definite increase in size relative to size of host is observed. However, during this period a well circumscribed circular area surrounding the original graft becomes elevated and more darkly pigmented than the normal ectoderm (Figure 2B). After about 46 hours this darkly pigmented area is considerably larger in diameter with the surface now thrown into marked folds and papillae (Figure 2C). Also, at about this time or slightly later, a small amount of tissue from the center of the growth becomes necrotic and is cast off. This tissue is of approximately the same size and at the same location as the original graft. During the third day the papillomatous growth increases in size to cover the major part of the host's flank.

The necrotic central area also becomes proportionately larger. Death occurs at the end of the third, or the beginning of the fourth day.

Serial sections of 15 experimental and 16 control hosts have been studied. In all of the controls and in all but six of the experimental animals, the graft tissue had healed perfectly forming a normal part of the host's ectoderm. In the six cases described above a papilloma-like growth had developed with the same arrangement of cell and cell components which obtains for papilloma tissue on the original overripe hosts (compare Figures 1C and 2D).

Length measurements were made of four of the six hosts bearing papilloma-like growths. At 2½ days after operation these were 7.3mm, 6.8mm, 7.0mm, and 7.5mm long. Twelve hours later they were respectively 7.6mm, 6.9mm, 7.2mm, and 7.8mm long. The increment during this period was therefore 0.1 to 0.3mm. The growth rate of 40 normal controls at the same stage of development was measured and found to vary from 0.45mm to 1.04mm with a mean of 0.73mm for 12-hour periods. Therefore, the six hosts bearing papillomas were definitely retarded in growth rate. The same is true for the three *Rana palustris* hosts which developed papillomas (see above) and of the overripe embryos which originally developed papillomas. Thus 34 of the papilloma-bearing donors used in these experiments varied in length from 3.5mm to 7.9mm (mean = 5.7mm) while normal controls were, without exception, significantly longer varying from 6.5mm to 12.0mm (mean = 9.7mm). These figures support an earlier interpretation of the progressive growth of papilloma tissue, which was made on the basis of mitotic frequency determinations (see Briggs, '41). Both sets of results indicate that the apparent progressive growth of the papilloma is due to retardation of the host rather than to excessively high proliferative rate of the growth itself. This interpretation would seem to hold as well for the papillomas developing on normal hosts following grafting, as for those developed originally on "overripe" embryos.

We have been concerned thus far with the behavior of papilloma grafts to the flank of hosts at tail bud stage. These comprise 63 of the total number of experimental animals (homoplastic). In the remaining 10 cases a small amount of papilloma tissue was inserted into the coelom through a short slit in the body wall of hosts at Stage 21 to 22 (8mm to 9mm). At this stage the gut is still large in diameter leaving but little space in the body cavity. Thus with a small glass rod the implanted tissue could be wedged firmly between splanchnic

and somatic mesoderm and, due to its dense pigmentation, could be observed through the body wall. After the operation the embryos were observed closely. The slit could be seen to close with the implant still in place in the coelom. During the first two days after operation the implant was observed through the body wall; it remained at approximately constant size while its pigmentation appeared to decrease in intensity. Thereafter, observation of the living tadpoles was impracticable without anaesthesia which was not undertaken. After 28 days the larvae (about 18mm) became moribund. They were then carefully examined under the dissecting microscope. The implant had apparently been resorbed for it could not be found at the original site and there were no growths elsewhere.

2. *Anterior Chamber of Adult Eye (67 cases)*

Papilloma tissue was implanted through a slit in the cornea and was manipulated into position on the iris by means of pressure applied to the outer surface of the cornea with a blunt glass rod. The grafts usually became attached to the iris. The hosts were kept at 15° C. During the subsequent two months the implants gradually resorbed and no growths appeared during the whole period of observation (7 to 8 months).

3. *Transplantation of Papilloma Tissue Subcutaneously to Tadpoles (102 Cases)*

Papilloma tissue was implanted into tadpole hosts ranging in length from 20mm to 40mm. Three sites were used: (*a*) dorsal subcutaneous tissue at the base of the tail, (*b*) subcutaneously behind the ear, and (*c*) subcutaneously in the mid-dorsal trunk region. Hosts were reared at 20°-22° C. For the first three or four weeks the implants were visible through the skin. Resorption gradually took place and they were no longer visible after four to six weeks. No growths appeared elsewhere in the body.

D. Discussion

From the results presented above it is evident that the growths appearing during the development of overripe *Rana pipiens* eggs are not malignant. Transplants of the most vigorous type of growth (the ectodermal papilloma) to various subcutaneous sites in tadpoles and to the anterior chamber of the eye of adult frogs gave no indication of further growth, although 169 such transplants were made.

It is, of course, possible that failure to progress was due to the absence of adequate vascularization since this seems to be so important a factor influencing the establishment of grafts in mammals (Foulds, '40). At the same time it indicates that the malignant behavior of the transplant reported by Witschi was conceivably an isolated case or that there is a profound difference in the nature of the growths produced by overripening in *Rana temporaria* and *Rana pipiens*.

Yet in *Rana pipiens* ectodermal papillomas do appear on embryos developing from overripe eggs and behave toward them, at least, in a pseudo-malignant manner. Such behavior could be due to abnormally rapid growth of the papilloma tissue or to retardation of the growth of the host embryo. Measurements of growth rates and mitotic indices show that the growth rate of overripe embryos bearing papillomas is significantly retarded while the papilloma itself grows at approximately the same rate or slightly slower than comparable ectoderm of normal embryos. Thus we may think of the papilloma as an island of ectoderm growing at a normal rate and spreading progressively over an abnormally slow-growing host. According to this interpretation we should expect papilloma tissue to behave as normal tissue when grafted to normal hosts. This expectation is borne out by the results of grafts to the flank of embryos. In the case of heteroplastic grafts the papilloma can be observed as it is incorporated as a normal part of the host ectoderm. The results from homoplastic grafts are the same and we may conclude that the papillomas tested are not malignant. At least their character is not irreversibly altered for when placed in normal surroundings they again assume the rôle of ordinary ectoderm.

In a small number of cases papillomas appeared on normal embryos after they had received grafts from "overripe" donors. In the heteroplastic experiments the papillomas which developed were made up of host tissue; also the hosts were retarded in growth rate as were the few homoplastic hosts which developed papillomas. Thus there is no evidence for continued progressive growth of the grafted papilloma tissue. These exceptional cases can again be explained as due to host retardation.

E. Summary

A progressively growing papilloma-like growth of the ectoderm develops on a small percentage of *Rana pipiens* embryos following delayed fertilization. When transplanted to the anterior chamber of adult frog eye or to subcutaneous tissue of tadpoles this growth regresses.

Grafts to the body cavity of 8mm to 9mm embryos behave likewise. Homoplastic and heteroplastic grafts to the flank of embryos at tail bud stage are incorporated as normal ectoderm. In a few exceptional cases hosts which had received flank grafts later developed papillomas, but these appeared to be composed of host ectoderm. Also, the hosts concerned were retarded in growth rate as are "overripe" donor embryos bearing papillomas. From these results we may conclude that the papilloma grows progressively only on retarded hosts and that when placed in normal surroundings it assumes the rôle of normal host ectoderm.

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THE PRENATAL GROWTH OF THE CAT: XI. THE WEIGHT OF THE INTEGUMENT IN THE FETUS AND IN THE ADULT CAT

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The skin covering the entire body with its many and very important functions, has received but little attention so far as its weight is concerned. In this paper, the increase in weight of the integument during the fetal period will be shown for both body weight and for body length and also the weight of the skin in the adult male and female cats. The weights of the integument as percentages of the body weight will be given.

The description of the specimens and methods of dissection and of determining the empirical formulae have been given (Latimer and Aikman, '31; Latimer, '33 and '36) and these details will not be repeated. The integument was carefully removed from 229 fetal, 35 newborn, and 104 adult cats equally divided as to sex. The skin, the fur, and the horny claws were always weighed together. Care was exercised not to include any subdermal fat and the mammary glands of the adult females were not included. The same methods were used for all specimens, except that the fetal and newborn cats had been preserved in formalin and the adults were dissected and weighed in the fresh state. The integument of each fetal and newborn cat was weighed in a glass stoppered weighing bottle on a chemical balance sensitive to 0.1 of a milligram. A laboratory balance sensitive to 0.1 gram was used in weighing the adult skins, and these skins were not weighed in weighing bottles, but were rolled up with the fur outside so as to prevent as much drying as possible during the weighing. The usual statistical formulae (Dunn, '29) were used in studying the adult cats.

I wish to express my appreciation of the very careful and accurate work of Mr. Douglas J. Malone in assisting with the statistical data on the adult cats.

A. Fetal Cats

The growth in weight of the integument of the fetal cats plotted on body weight is shown as the line beginning at the left in Figure 1

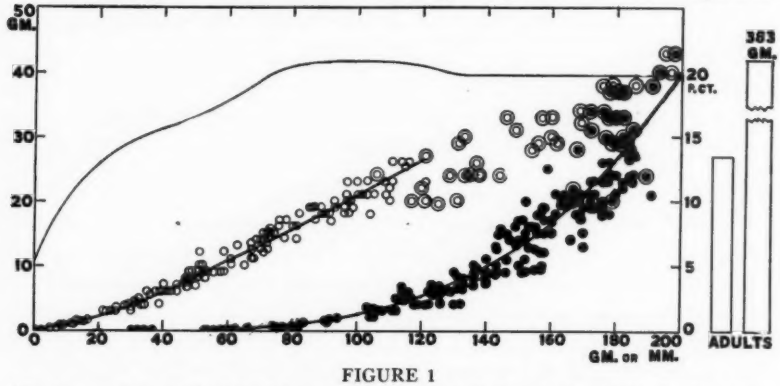

FIGURE 1

The increase in weight of the integument in grams plotted on body weight also in grams is shown in the curve starting at the left and with the individual skin weights shown as circles for the fetal cats and as double circles for the newborn cats. The weights of the same integuments plotted on body length in millimeters are represented by the curve starting farther to the right and with the fetal skins shown as dots and the skins of the newborn cats, as dots enclosed by circles. Formulae for the curves are given in the text. The lighter line without any cases represents the percentage weights of the integument plotted on body weight. The percentage values are given at the right and the weights in grams at the left. The shorter column at the right represents the percentage of the average adult male integument and the broken column, the average weight of the adult male integument.

and with the weights of the individual skins of the fetal cats shown as circles, and the skins of the newborn cats, as double circles. This curve was drawn from the following empirical formulae; from 3 to 50 grams of body weight,

$$Y = \frac{X^{1.3}}{18.4} - 0.01X + 0.04, \text{ and from 50 to 120 grams,}$$

$$Y = 0.25\ (X - 50) + 8.327.$$

The curve is not shown in the figure, but it was found that the following formula fitted the newborn cats very well, or from 120 to 200 grams of body weight,

$$Y = 0.24X - 6.80.$$

In the above formulae, Y represents the weight of the integument in grams and X, the body weight also in grams. The average percentage deviation of the calculated from the observed values for each 10

grams increase of body weight, or 10 millimeters increase in body length for the preceding formulae, was 2.18 for the fetal cats and 1.45 per cent for the formula for the newborn cats.

The curve starting farther to the right and with the individual cases shown as dots for the fetal cats and as dots enclosed by circles for the newborn cats, represents the weights of the integument plotted on body length. The formula for this curve from 60 to 200 millimeters of body length is,

$$Y = \frac{0.1X^4}{3976} - 0.2.$$

In this formula, Y again represents the weight of the integument in grams, and X, the body, or nose-anus length, measured in millimeters. The smallest specimens measured only 30 mm. in length and this formula does not accurately fit these smallest specimens. From 30 to 60 millimeters of body length the growth of the integument was irregular and less rapid. The newborn kittens are included in this formula. The average percentage deviation of the formula is 6.37 per cent, a figure larger than for the formulae based on body weight but still a comparatively small percentage deviation.

The lighter line without any cases represents the weight of the integument as a percentage of the total body weight. The percentage values are shown in the right margin. This curve shows that the integument increases from about five per cent in the smallest fetuses to a little over 20 per cent in the oldest fetuses. This drops to a little less than 20 per cent in the newborn cats and to 13.42 per cent in the adult males as shown by the shorter of the two columns at the right of the graph and marked "adults" below the columns. The taller column represents the average weight in grams of the adult male integument. The decrease at time of birth is shown in the integument weights plotted on body weight, for there is an appreciable decrease between the calculated values for the fetal curve and that for the newborn cats. There is a difference of 3.8 grams or a drop of 14.8 per cent from the curve of the fetal cats. When the decrease in the relative weight of the integument between birth and the adult cats occurs we have no knowledge, and so far as is known no work has been done on this problem. In the curve based on body length, these same data of the newborn cats seem to be slightly above the line for the fetal cats although they fall within the same limits of percentage variation as do the fetal integuments.

When the specimens were being dissected and weighed, the degree of development of the hair and vibrissae was recorded on the original data cards and from these data we can gather an idea of the development of the fur. In the fetuses of three grams of body weight the vibrissae were short but they had already emerged through the skin. The skin was hairless but there were rows of papillae formed by the developing hairs. The hairs were first seen piercing the skin at 23 grams of body weight and by 35 grams of body weight most of the fetuses had the hair erupted, although it was short. The color of the fur was evident in some of the 50-gram fetuses and by the time they had attained 75 grams of body weight the fur was well developed. In all cases the vibrissae preceded the development of the fur. If these body weights are studied in connection with the percentage curve in Figure 1, it will be evident that the most rapid increase in relative weight of the integument occurs preceding the eruption of the fur. The slightly depressed portion of the percentage curve centering at about 50 grams of body weight occurs when the fur is nearly half grown. This depression in this curve may be due to the more rapid growth of some other system. The percentage curve for the weight of the digestive tube (Figure 1, Latimer, '34) shows a similar but slightly less evident depression centering at about 50 grams of body weight.

B. Adult Cats

The average weights in grams and the average percentage weights of the integument of the 52 male and 52 female cats, together with their probable errors are shown in Table 1. The coefficients of variation are also given, and in the absolute weights and in the percentage weights the males are more variable. The significant ratios given in the last column of this table show that both the absolute weight and the percentage weight of the integument are significantly greater in the male cats.

The body weight increases 200 times (0.6 to 120 grams) and during the same time, or from the beginning of the fetal period to birth, the integument is increasing 698 times. The integument of the male increases 14.8 times from birth to maturity and the similar increase for the female is 12.06 times. If these increases are compared with the total body increase in weight we find that during the fetal period the integument increases 3.49 times as much as the increase in the body weight. In postnatal life the increase in the male body weight is 1.59

TABLE 1

ABSOLUTE WEIGHTS AND PERCENTAGE WEIGHTS OF THE INTEGUMENT IN THE ADULT CATS

	Weights in grams	Coefficients of variation	Difference P.E. diff.
Male cats	383.1±11.4	31.80±2.31	5.63
Female cats	311.5± 5.65	19.39±1.33	
	Percentage weight		
Male cats	13.42± 0.11	9.15±0.61	3.52
Female cats	12.89± 0.10	8.04±0.54	

times as much as the increase of the integument and for the females the ratio is 1.69. Hence we see that the integument increases more than the body weight during the fetal period and not as rapidly as the body weight in postnatal life.

There are very few data on the weights of the integument of the cat in the literature. Sedlmair ('99) gives the weight of the integument of one female cat and reducing this to percentage of the body weight it is 14.63 per cent. Welcker and Brandt ('03) give the average percentages of the integument in three females and one male cat as 13.33 per cent. All of these are easily within the range of the values of this series of cats. Jackson and Lowrey ('12) find that the skin in the rat forms 17.95 per cent of the body weight, a larger percentage than in the cat. They also have gathered the data from other workers for many of the smaller animals and for many of the larger domestic animals. In general the smaller animals have relatively heavier skins than the cat, but the larger domestic animals have relatively lighter skins.

To better determine the weight of the integument from cats obviously above or below the average size, regression lines were drawn and simple empirical formulae developed so that the weight of the integument could easily be calculated from either body weight or body length. The formulae were developed in a manner similar to that used for the fetal cats, but the body weights were averaged for each 500 grams increase in body weight, and for each 25 millimeters increase in body length. This, it seems, is a more accurate method than by the use of the average weights as given above. The weights of the integument of the males and of the females were plotted on both body weight and on body length and the formulae for these regression lines are as follows. For the males from 1700 to 4500 grams of body weight, $Y = 0.16X - 67$. For the females from 1500 to 3500 grams

of body weight, $Y = 0.11X + 42$. The average percentage deviation of these formulae for the males is 3.29 per cent and for the females, 0.40 per cent. In these formulae Y represents the weight of the integument in grams and X, the body weight also in grams.

For these integument weights plotted on body length in millimeters the formulae are as follows; for the males from 450 to 600 mm. of body length, $Y = 2.48X - 906$, and for the females from 450 to 570 mm., $Y = 1.5X - 455$. In these formulae, Y again represents the skin weight in grams and X, the body length measured in millimeters. The average percentage deviations of these formulae are 5.01 per cent for the males and 3.75 per cent for the females. All of these curves are rectilinear and it does not seem necessary to reproduce them here.

The percentage weights of the skin of both the males and the females were plotted in a similar manner on the body weight and lines drawn through the averages. Both of these are straight lines but the line for the males increases from about 12.4 per cent at 1700 grams of body weight to about 15.0 per cent at 4500 grams. The line for the females, starts at 13.5 per cent at 1500 grams of body weight and decreases to 12.2 per cent at 3500 grams of body weight. The two lines intersect at 2320 grams of body weight. The only explanation seems to be that the skin does not change in the female and with added weight it naturally decreases in percentage. In the males, however, the fur was often noticed to be heavy and the skin tough and many of the older toms carried evident marks of physical combat. This rising percentage value of the male integument must be due to the necessary protection which the older and less agile animal must have in maintaining its life against its adversaries, or at least its standing in its community.

The correlations between the skin weight and the body weight, body

TABLE 2

CORRELATIONS WITH THE WEIGHT OF THE INTEGUMENT

	52 male cats	52 female cats
Body weight	+0.974±0.0044	+0.945±0.010
Body length	+0.845±0.027	+0.673±0.051
Kidneys	+0.860±0.024	+0.811±0.032
Liver	+0.602±0.060	+0.517±0.069
Digestive tube	+0.719±0.045	+0.456±0.074
Small intestine	+0.640±0.055	+0.356±0.082
Large intestine	+0.690±0.049	+0.526±0.068
Lungs	+0.600±0.060	+0.227±0.089

length and the weight of six of the internal organs, for both the males and the females, are shown in Table 2. As has been found for most of the measurements of these adult cats, the males are more variable and yet the correlations are higher than for the females. The averages of these correlations in Table 2 are 0.741 for the males and 0.564 for the females or the average is 31.4 per cent greater in the male cats. The lowest correlation in both sexes is with the lungs. The digestive system and its parts are not as well correlated as are the kidneys. In fact the kidneys are better correlated with the weight of the skin than is the body length. All of the correlations are positive but some of the correlations with the weight of the female integument are too low to be significant.

C. Summary

Empirical formulae have been developed whereby the weight of the integument may be estimated from either the body weight or the body length, for the fetal, the newborn, and for the adult male and female cat. The average, the coefficient of variation, and the significant ratio have been determined for the male and female adult cats.

The integument of the adult male cat is more variable in both absolute weight and in percentage weight and it is also significantly heavier in both absolute and in percentage weight than the female.

The vibrissae appear through the skin before the hair, which is evident as rows of papillae until it emerges through the skin from 23 to 35 grams of body weight. By 75 grams of body weight the fur is well developed.

The integument forms about five per cent of the body weight in the smallest fetuses. This increases rapidly at first and then more slowly, with a retardation at about 50 grams of body weight, until the maximum of a little over 20 per cent is attained at birth. A postnatal decrease is shown in the newborn and the percentage in the adults is about 13 per cent.

The weight of the adult integument is well correlated with body weight and with kidney weight in both sexes. The correlations average a little over 31 per cent better in the males, although the male integuments are more variable in both absolute and percentage weights.

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THE WEIGHT OF THE HYPOPHYSIS IN THE DOG

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The weight of the entire human hypophysis as well as of its parts has been very thoroughly studied by Rasmussen ('24, '28, and '34). The rat hypophysis in its postnatal growth has been given by Donaldson ('24) and the weights of the fetal and adult cat hypophyses have been measured by Latimer ('39a and '39b), but so far as is known there are no data on the weight of the dog hypophysis. In addition to these quantitative studies many studies have been made on the physiology of the hypophysis and in these studies very often quantitative data are given for the control animals. Lauson, *et al.* ('37) give the hypophysis weight in 36 control rats and there are many similar papers, but no attempt will be made to review all of this literature. Rasmussen's papers give an excellent review of the literature on the weight of the human hypophysis.

The hypophyses from 155 male and 151 female dogs were removed from the sella turcica after the brains had been removed for another study. As the brain was removed, after the top of the calvarium had been removed, the nerves from the brain were cut and at this time the stalk of the hypophysis was cut. The stalk of the hypophysis was severed close to the mass of the gland but no attempt was made to remove the meninges. These hypophyses were immediately put in a moist chamber until transferred to glass stoppered weighing bottles and weighed on a chemical balance sensitive to 0.1 milligram. The dogs had been used in the physiology department for experimental work, but only those dogs were used which were mature and apparently in good health and which had been used for only short experiments in which the weight of the hypophysis was not affected. In no case were dogs used which had served for prolonged experiments in which the general condition of the animal was affected. These dogs were indeed a random selection and no selection of the dogs from the laboratory was made except in selecting only mature dogs, and toward the end, only females were taken to more nearly balance the numbers of the two sexes.

The body weight of each dog was the weight taken at the beginning of the experiment, on a platform balance sensitive to ¼ of a pound. It was very frequently impossible to reweigh these dogs due to the loss of blood or other body fluids during the course of the experiment. The body length, or nose-anus length was measured with a flexible steel tape graduated to 1/10 millimeter, and was measured from the tip of the nose to the anus. The tape was held close to the contour of the head, neck, and body. The original body weights in pounds were converted into the metric system and all of the rest of the data were taken in the metric system. The dogs were taken at various times from October, 1936, to July, 1939. The removal of the brain, cord, and hypophysis was done in part by several medical students, but the final cutting of the stalk and the weighing of the gland was done by the author.

I wish to express my most hearty appreciation of the kindness of Dr. O. O. Stoland and the other members of the Physiology Department for permitting the use of these dogs. I also wish to thank the following students who helped in the removal of the brains, spinal cords, and the hypophyses from these dogs; E. P. Sereres, L. L. Holbert, M. H. Noltensmeyer and R. R. Remsberg. To Mr. Douglas J. Malone I wish to express my appreciation of his assistance with the statistical work.

A. Weights

The average weights in grams and the coefficients of variation of the male and female hypophyses are shown in Table 1. The usual formulae, as given by Dunn ('29), were employed in determining all of the statistical constants in Table 1. The second two lines give the average and coefficient of variation of the weights of the hypophyses reduced to percentages of the body weight. The last column gives the significant ratios and these show that although the female hypophyses are on the average slightly heavier, yet they are not significantly heavier. The percentage weights are significantly heavier in the females as shown by the ratio of 10.31. It is also interesting to see that the variation of the percentage weights is less than for the absolute weights.

The third division gives the average body weights and the last two lines the similar data for the body lengths. The two highest coefficients of variation are for the body weight of the male and the female dogs. This is to be expected in a group of dogs ranging from 4 to 30 kilograms in body weight. The coefficients of variation of the body lengths are also high for linear dimensions. Both body weight

TABLE 1

WEIGHTS AND PERCENTAGE WEIGHTS OF THE HYPOPHYSIS IN 155 MALE, AND 151 FEMALE DOGS

	Average weight in grams	Coefficient of variation	$\frac{Diff.}{PE_{diff.}}$
Male dogs	0.0658±0.0012	32.29±1.36	0.66
Female dogs	0.0670±0.0014	38.87±1.72	
	Percentage weight		
Male dogs	0.000649±0.0000097	27.51±1.13	10.31
Female dogs	0.000793±0.0000095	21.89±0.89	
	Average weight kilos		
Body weight, males	11.00±0.26	44.75±1.98	6.07
Body weight, females	8.93±0.22	46.13±2.08	
	Average length centimeters		
Body length, males	81.9±0.58	13.40±0.51	6.03
Body length, females	76.8±0.61	14.77±0.57	

and body length are significantly greater in the males and this will explain why the hypophyseal weights, slightly greater in the female, are significantly greater when expressed as percentages of the body weights.

The wide range in body size of these dogs, which were of several different breeds and many of indeterminate breed, makes the value of these average weights of the hypophyses somewhat unreliable. They are given here because they were needed for obtaining some of the later statistical constants, and also the last two columns do give us some idea of the variability and the sex differences in these hypophyses. From these data we can see that the weights of the hypophyses are greater in the female dogs, as has been found for the human hypophyses (Rasmussen, '34), and the rat (Donaldson, '24). In the cat, the average absolute weight of the male hypophysis is significantly greater, and the percentage weights are slightly but not significantly greater in the females (Latimer, '39b). The hypophysis of the dog is less variable than the body weight.

As a much more accurate method of determining the weight of the hypophysis from either body weight or body length, the following formulae for regression lines are presented. The averages and percentages in Table 1 are valid, of course, for dogs of average size but for all other dogs the formulae will give much better estimates of the weight of the hypophysis.

The weights of the hypophyses in grams were plotted against body weight in kilograms. The average body weight of all dogs in each two kilogram range was determined and also the average weight of the hypophyses in each of these groups and this common point of average body weight and average hypophysis weight was plotted on the preliminary graph. There were seven dogs in the last group and this group ranged from 22 to 30 kilos of body weight. Similar methods were used for plotting the weights of the hypophyses on body length, except that the body lengths for each 10 centimeters of body length were averaged as were the body weights. The last group including only three dogs extends from 110 to 135 cm. of body length.

The formulae for the weights of the hypophyses in grams plotted on body weight for the male dogs from 4 to 28 kilos of body weight, is: $Y = 0.0031X+0.032$, and for the females from 4 to 24 kilos, $Y = 0.0051X+0.0211$. In these formulae Y represents the weight of the hypophysis in grams and X, the body weight in kilograms. The average percentage deviation of the calculated from the observed values for the averages for each two kilograms increase in body weight is 4.52 per cent for the males and 2.87 per cent for the females.

The male hypophyses plotted on body length from 65 to 115 centimeters of body length may be determined from the following formulae: $Y = 0.0017X - 0.0717$ and for the females from 55 to 110 centimeters of body length, $Y = 0.0015X - 0.05$. In these formulae Y again represents the weight of the hypophyses in grams, and X now represents the body length measured in centimeters. The average percentage differences for these formulae are 5.50 per cent for the males and 5.53 per cent for the females.

These curves are all rectilinear and to save space they are not given here. There is an average amount of scattering of the individual cases but still it is felt that by solving these simple formulae far more accurate estimates of the weights of the hypophyses may be determined than by the use of the average weights or the average percentage weights given in Table 1.

The percentage weights of the hypophyses were plotted on body weight in the same manner as the absolute weights and the two curves in Figure 1 show the changes in percentages of the hypophyses with reference to the body weight for the males and for the females. The upper curve represents the percentages of the female dogs and the lower, that of the males. The relative position of the two curves shows that the percentage weights of the female hypophyses are greater at all

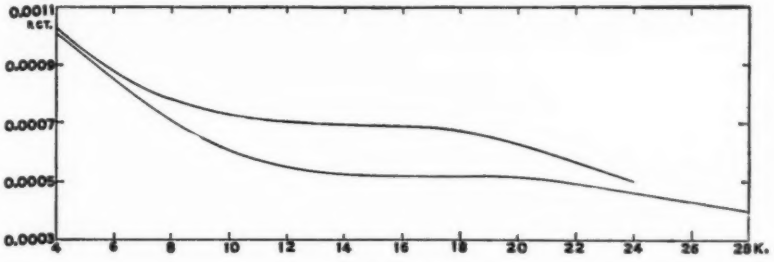

FIGURE 1

The percentage weights of the hypophyses of the female dogs are represented by the upper curve terminating at 24 kilos of body weight and the percentages of the male dogs in the lower curve. These percentages of the body weight are plotted on body weight in kilograms and the percentages of the body weight are shown at the left.

body weights, although in the smallest dogs and again at 24 kilos of body weight there is little difference in the percentages. At four kilos of body weight, the hypophyses of the female dogs average 0.00103 and for the males the curve shows 0.00101 per cent and at 24 kilos of body weight, the end of the curve for the females, the values are, 0.0005 for the females and 0.00046 per cent for the males. The greatest difference in the percentages is found in the dogs of medium size or from about 10 to 20 kilograms of body weight.

In general, the two curves are similar and they show that the hypophysis is relatively heaviest in the smallest dogs, with a horizontal portion in the middle range of body weight, and again relatively lighter in the largest dogs.

B. Correlations

The correlations of the hypophysis weight with the body weight and length, with the brain, with seven of its divisions, and with the weight and length of the spinal cord are shown in Panel *A* of Table 2, for both the males and the females. The average of the 12 correlations for the females is 0.748 and for the males, 0.670. or in general the correlations with the female hypophysis are higher than for the male. The two sexes show a marked similarity in the correlations, for in both sexes the highest correlation is with the body weight, followed in the same order in both sexes by the cord length, body length, and cord weight, and in both sexes the lowest correlation is with the mesencephalon. All of the correlations are positive and all above +0.5 except that between the male hypophysis and the mesencephalon.

TABLE 2

CORRELATIONS WITH THE WEIGHT OF THE HYPOPHYSIS

	Males (155)	Females (151)
A. *In the dog*		
Body weight	+0.796±0.020	+0.873±0.013
Body length	+0.738±0.025	+0.797±0.020
Brain weight	+0.687±0.029	+0.740±0.025
Olfactory lobes	+0.544±0.038	+0.702±0.028
Hemispheres and diencephalon	+0.682±0.029	+0.692±0.029
Prosencephalon	+0.692±0.028	+0.712±0.027
Mesencephalon	+0.469±0.042	+0.654±0.031
Cerebellum	+0.620±0.033	+0.684±0.029
Medulla	+0.664±0.030	+0.771±0.022
Rhombencephalon	+0.656±0.031	+0.742±0.025
Cord weight	+0.735±0.025	+0.773±0.022
Cord length	+0.756±0.023	+0.835±0.017
B. *In the adult cat*		
	Males (52)	Females (52)
Body weight	+0.189±0.091	+0.434±0.077
Body length	+0.165±0.092	+0.465±0.074
Brain weight	+0.214±0.090	+0.510±0.070
Prosencephalon	+0.162±0.092	+0.484±0.072
Mesencephalon	+0.249±0.089	+0.457±0.075
Cerebellum	+0.231±0.089	+0.455±0.075
Medulla	+0.162±0.092	+0.473±0.073
Cord weight	+0.165±0.092	+0.494±0.071

In an earlier paper, the correlations between the weight of the hypophysis and the body weight and the body length in the cat have been given (Latimer, '39b) and both of these are much lower than the corresponding correlations in the dog, and so the data used in preparing the report on the cat nervous system (Latimer, '38) was used to get correlations comparable to these given in Panel *A* of Table 2 for the dog. The correlations between the cat hypophysis weight and the body weight and length are copied from the earlier paper on the endocrine glands (Latimer, '39b), and the correlations of the hypophysis with brain weight, with the four divisions of the brain, and with the weight of the cord were computed and are shown in Panel *B* of Table 2.

The only points of similarity in the correlations in Panel *A* and in Panel *B* are that in both, all of the correlations are positive and they average higher for the females. The correlations with the male cat hypophyses average but +0.192 compared with the average of +0.670 for the dog, and in several of these correlations for the cat the probable error is over one-half the value of the correlation. Hence we may conclude that the hypophyses in the male cat are not significantly

correlated with any of these parts of the nervous system nor with the body weight or body length. The correlations for the female cats average +0.472, which is very low but higher than that for the males. It again is much lower than the average of the correlations for the hypophyses of the female dogs. In the male cats the best correlation is with the mesencephalon, and in the females the best correlation is with the brain weight and this correlation between the weight of the hypophysis and the brain weight is the only one of the 16 correlations for the cats which is above +0.5 per cent.

In general we may conclude that in both the dog and the cat the female hypophysis is better correlated with body weight and body length, and with the brain and its parts, and with the spinal cord. In both sexes, all but one of the correlations are significant for the dogs, and there is but one correlation in all of the cats which may be considered significant. It would be very interesting to be able to compare correlations of the hypophysis weight and the weights of the several endocrine glands in the dog, and see if they would be higher than the correlations which have been found for the cat. The dog hypophysis is quite well correlated with the weights of the nervous system and with body weight and body length.

C. Summary

Empirical formulae are given for computing the weight of the hypophysis from either the body weight or the body length for the male and female dogs. It is felt that this is a far more accurate method than by the use of the averages or the average percentage weights.

The hypophyses are slightly heavier in the female dogs but the weights of the hypophyses as percentages of the body weight are significantly heavier in the females. Both the body weight and the body length are significantly greater in the male dogs.

The body weights are more variable than the absolute weights of the hypophyses and the least variable are the hypophyses as percentages of the body weight.

The hypophyses are relatively heaviest in the smallest dogs and relatively lightest in the largest dogs.

The weights of the hypophyses in the dog are well correlated with body weight and length, with the brain and its divisions, and with the weight and length of the spinal cord. Correlations of the cat hypophysis with similar measurements are all very much lower, or the cat hypophysis is not well correlated with these dimensions. The cor-

relations average higher in the females than in the males for both the dog and the cat.

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THE SCALE OF BEING ACCORDING TO THE POWER FORMULA

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Otto Snell in 1891 applied the equation $Y = bX^k$ to an evaluation of brain-body weight relationships. In 1898 Dubois and independently Lapicque made determinations of "*k*" and "*b*" values for brain-body weight relations in a series of animals. In 1919 Klatt applied the equation to heart-body weight data. More recently Huxley (1932) compiled the findings of many workers in the field of relative growth. Hersh (1934) has applied the formula to relative skull growth in the titanotheres. In 1938 I applied the equation to brain, heart, thyroid, and adrenal body weight relations in a series of ungulates. Brummelkamp in 1938 observed an interesting regularity in "*b*" values for primate brains. Lumer (1937) discussed the consequences of sigmoid growth for relative growth functions. In a recent study Zipf (1941) has pointed to the regularity of size increase in American cities and apparently this growth may be expressed by the relative growth equation.

The present study is an attempt to determine "*b*" values for brain, thyroid, adrenal, and heart in a wide range of animals and to set up a scale of being based on numerical values of "*b*."

Even a superficial examination of the ratios of glands or organs to body weights in various vertebrates indicates that as the animal increases in weight the subordinate part commonly fails to keep pace with the body weight increase but advances at a lower rate. Thus the ratio of brain to body weight is ordinarily higher in a small than in a large animal, with the exception of the primates and man, even though the brain may be more highly developed in the large animal. Likewise, the heart, thyroid gland, and the adrenal gland weights fail to maintain the same rate of increase as the body in the large compared with the small animal.

A. STANDARD CURVES

In view of changing mass-surface relationships, how can valid com-

parisons of the size of the various organs and glands in animals of different body weights be made? For example, if the brain/body weight ratio in the lion is 1:739 and in the cat it is 1:453, what can we conclude from such relative ratios? If we could rule out the factor of body weight in each case, that is, if we could relegate body weight to a position in which it does not interfere with a true valuation of a subordinate part, then the glands of a 100 gram animal could be effectively compared with those of a 10,000 gram animal. Such a comparison can be made. This is due to the regularity of growth and size increase in the animal organism. The animal is not a hit or miss affair, but represents the orderly working together of a number of systems resulting in effective work and activity, and this organization of systems maintains itself for a longer or shorter period as a self-sustaining entity. To establish the nature of these various regularities in the bodily mechanism is one of the central tasks of biology, for an analysis of these regularities, if carried far enough, should lead to a knowledge of the fundamental laws of organic growth and explain the scale of being.

One of the first individuals to point out the regular nature of the increase in size of a subordinate part was Otto Snell, who in 1891 discovered that the brain/body weight relationship in animals of various species could be described graphically in terms of what the mathematicians call the *Power Formula,* which in equational form reads $Y = bX^k$. This implies that the brain weight, Y, is equal to the body weight, X, raised to the k power times a constant b, or that the brain increases at one rate and the body at another, but that this ratio of increase is regular and is equal to k.

When such a brain/body relationship is plotted on a double logarithmic graph, a straight line relationship is approached which passes through the various plotted points and the slope of the line is indicated by the power K (Figure 1). If this relationship holds, it means that a valid comparison between the largest and the smallest member of a species or of a closely related group may be made, since the effect of the larger body is placed on the same basis as that of the smaller body.

We have applied this formula to the weight data of a number of vertebrates, specifically to brain-thyroid, adrenal gland, heart, liver, kidney, lung body weight relationships. The extent to which regularities were observed in brain, thyroid gland, adrenal gland, heart-body weight relationships forms the subject for this study. "K" values

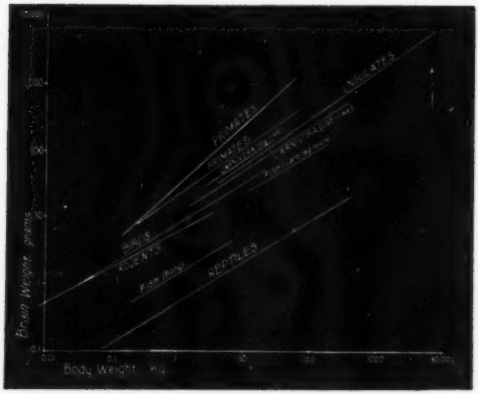

FIGURE 1
BRAIN-BODY WEIGHT RELATIONS IN VARIOUS VERTEBRATE CLASSES

were determined for the animal groups indicated in Tables 1 to 35 as follows: brain, 541; thyroid, 836; adrenal, 867; heart, 850. While deviations from these values were large in many instances, sufficient regularity was observed to indicate a fundamental principle of size increase. With these values as a starting point, it becomes possible by the use of b to establish a scale of being in numerical terms. This represents an extension of the cephalization coefficient of Dubois (1898).

If these regularities are valid, then we gain an extremely valuable standard by which to compare a given animal with his fellows. Suppose, for example, that one wishes to compare the brain, heart, adrenal gland, and thyroid gland of the lion with the same glands of other catlike carnivores. By drawing a brain curve with a slope of .541 (k) (Figure 2), and a b value of .3710, the average for the group, and by setting up similar curves with proper values of b and k for the other glands, one may tell at a glance the position of the lion, as far as these important glands are concerned. Note, in comparison to his fellow catlike animals, that his cephalization coefficient is .4471 against .3710 for the rest of the group.

It may be objected that this is the usual way of making a comparison, namely, by noting the deflection of a given set of values from those established for a group. This method, however, has the advantage of comparing an individual record against a standard curve

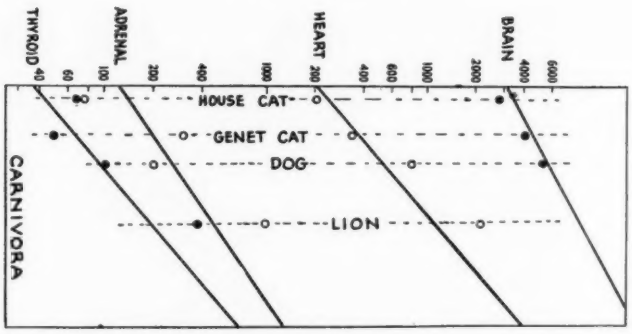

FIGURE 2

CURVES EXPRESSING BRAIN-THYROID, ADRENAL AND HEART RELATIONSHIPS TO BODY IN CARNIVORA

whose slope is common to the vertebrates generally. The deflection of the points established for the lion from the curve established for the group permits the inference that certain fundamental differences exist in lion physiology or behavior compared to the catlike group.

In the house cat, the brain falls slightly below the standard curve, the heart is about on the line established for the order, the adrenal gland is low in comparison with the standard, and the thyroid gland is relatively high (Figure 2). As a matter of fact, the brain value (*b*) for the cat is .3272 (9 specimens) as compared with .4471 for two wild African lions; the value for the heart of these same cats is .1475 as against .3306 for the lions. These deflections in the cat may but reflect the effect of domestication in this carnivore. In any event, they permit the deduction that pound for pound the cat has not the same energy pattern as has the lion, since on this scale the brain, thyroid gland, adrenal glands, and heart of its wild relative have somewhere along the line experienced a more rapid relative growth.

These examples illustrate the principle which was used to evaluate the gland pattern of animals of various types. The variations in thyroid gland, adrenal gland, and heart coefficient appear to be more than chance deviations, for they are regular in their appearance. Thus, the brain coefficients of animals of the same body weight but of different orders are regular in their differences. The brain coefficient for the dog, for example, is on a definitely higher level than is that of the cat. Moreover, these differences are reflected in the behavior pattern of the animal.

B. The Brain

Figure 3 is a graphic presentation of the power formula applied to

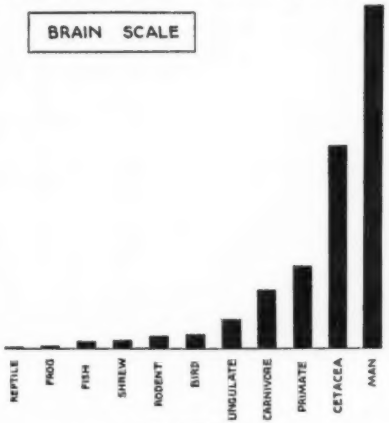

FIGURE 3

Degree of Cephalization Expressed by "*b*" in Various Vertebrates

the brain/body relationship. The graph indicates the degree of brain development or the position in the life scale of various groups of animals studied. The surprising fact becomes evident from this graph that the cetacea stand higher in cephalization than do primates with the exception of man, while carnivora stand about half as high as do the primates.

Another surprising fact is that the reptiles and the amphibians present a lower level of cephalization than do the fishes. If the fishes gave rise to amphibia and indirectly to the reptiles, one might assume that this evolution would also produce a larger brain. It appears from these calculations, however, that the aquatic life requires larger brain than does cold-blooded land-life. Unfortunately, this series does not include purely aquatic amphibia.

A comparison of the shrew and the mouse group (Figure 3) indicates the wide gulf which exists between the two, since the mouse stands at about twice the cephalization level as does the shrew.

The birds and the bats, curiously enough, as shown in Table 1, although widely separated from the standpoint of blood relationship, stand next to each other in brain development, although the comparison is not quite fair, since 458 birds are compared with only five vampire bats.

Measured by this yardstick, there is a wide gulf between the human

TABLE 1

B values (brain) averages Number of animals	Name	Position in the scale of being Average *b* value
188	Reptiles	.0055
6	Frogs	.0156
3	Fishes	.0751
68	Insectivores	.0743
450	Rodents	.1370
458	Birds	.1464
5	Vampire Bats	.1543
1177	Ungulates	.3247
84	Carnivores	.4035
443	Primates without Human	.8971
8	Cetacea	2.220
11	Human	3.625
2901		

being and the cetacea as opposed to the remainder of the backboned animals. To see this comparison graphically, let us place the reptiles on a pedestal of brain development .55 inches high. The cetacea then tower 22 inches above them, while the human being rises 362 inches above the reptile level (Figure 3).

Just what do such differences in brain development mean so far as energy output is concerned? Ordinarily it is assumed that a large brain implies a high degree of intelligence. These data show that the blue whale, the white whale, and the porpoise stand on a cephalization level not much lower than that of man. Man stands at a level of 3.62 on the chart (Figure 3), the cetacea stand at 2.22, while the primates, aside from man, fall as low as .8791.

It becomes apparent that the brain is related to the heat output according to a considerable body of our unpublished metabolism data, and heat output means energy output. The reptile, frog, and fish do not have sufficient brains to keep warm according to this concept, and it is only as more brain appears that the organism is able to heat its body above the temperature of its surroundings.

The values shown in Table 1 represent averages for particular orders of animals. Within these orders, however, there are wide ranges between individuals and species. Individual differences observed in a group like the reptiles or carnivores, for example, indicate the real value of this method. The skunk and the seal are both carnivores. Unless a value of .1533 established for the skunk brain is considered simply a chance variation from the value of .8188 deter-

mined for the ringed-seal brain, one must assume differences in brain development.

Table 2 shows the relative position of the carnivore group. The

TABLE 2
CARNIVORE BRAIN

Name	No.	*b* value	Name	No.	*b* value
Cat-like			*Dog-like*		
Domestic cat	1	.2847	Skunk	2	.1533
Genet cat	1	.2917	Skunk	1	.1841
Domestic cat	2	.3152	Mongoose	1	.3026
Genet cat	2	.3283	Police dog	1	.3151
Domestic cat	5	.3293	Bat eared fox	1	.3240
Domestic cat	2	.3392	Local dog	4	.3636
Tiger	1	.3443	Florida mongrel	2	.3696
Lion	2	.3588	Grizzly bear	1	.3801
Weasel	3	.3514	Coati	1	.3910
Weasel	1	.3596	Raccoon	1	.4164
Leopard	1	.3972	Raccoon	1	.4258
Tiger	1	.4001	Panama dog	1	.4325
Lion	3	.4024	Grey fox	2	.4346
Mountain lion	1	.4125	Greyhound	1	.4472
Spotted hyena	2	.4456	African dog	3	.4475
Lion	2	.4471	Husky dog	2	.4796
Serval cat	1	.4599	African dog	2	.4835
Serval cat	2	.4885	Raccoon	1	.5231
Jaguar	1	.5159	Russian wolf	1	.5257
Puma	1	.5378	Arctic white fox	1	.5482
			Arctic red fox	1	.5483
Average	36	.3710	Timber wolf	1	.5773
			Local dog	2	.5923
Seals and Walruses			Coyote	1	.6318
Bearded seal	1	.6310	Polar bear	1	.6638
Ring seal	2	.7448	Polar bear	1	.6745
Ring seal	2	.8188			
California seal	1	.8395	Average	37	.4361
Walrus	3	.8198			
Walrus	1	.9940			
Walrus juvenile	1	1.6210			
Average	10	8.0111			

average "*b*" value for cat-like carnivora is .3710; the bear- and dog-like carnivora is .4361, with the aquatic carnivora at .8051. While such an average has little meaning taken by itself because of the wide range of values, in this particular case the chance selected cat- and dog-like carnivora are about equal in number and indicate a definite trend.

The ungulates fall naturally into two divisions, the odd-toed and the even-toed groups. In the first group are such animals as cattle, pigs, antelope, and deer. In the second are horses, zebra, and burros. The elephant, although odd-toed, does not fall into this grouping. It

is included here because as a sub-ungulate it is not far removed from the ungulate group. When separated into odd-toed and even-toed groups, the values run as indicated in Table 3. The brain coefficient

TABLE 3
UNGULATE BRAIN

Name	No.	*b* value	Name	No.	*b* value
Even-toed			*Odd-toed*		
Holstein bulls (a)	5	.2797	Horse	1	.4083
Holstein bulls (a)	2	.2899	Horse	1	.4244
Steers (a)	18	.2953	Rhinoceros	1	.4304
Holstein cows (a)	200	.3106	Burro	1	.4357
Holstein bulls (a)	194	.3179	Burro	1	.4748
Holstein bulls (a)	5	.3184	Tapir	1	.4810
Warthog (a)	1	.3184	Mules, Panama	2	.4882
Cows, misc.	71	.3344	Horse	1	.4983
Jersey, male	2	.3349	Horse	1	.5069
Jersey, male	10	.3354	Horse	10	.5128
Ayrshire, female	44	.3404	Horse	1	.5285
Guernsey	62	.3438	Mule	4	.5292
Hippopotamus	1	.3472	Horse	1	.5327
Giraffe	1	.3472	Horse, Panama	31	.5482
Guernsey, female	217	.3552	Horse, thoroughbred	4	.5805
Steinbok	2	.3677	Horse, thoroughbred	2	.5860
Jersey, male	213	.3738	Horse, thoroughbred (a)	3	.6163
Jersey, male	2	.3749	Zebra	2	.6431
Dik Dik, male	1	.3873	Burro	1	.6471
Gazelle, Thomson's	2	.3879	Elephant	1	1.0500
Reedbuck	1	.3992	Shetland pony	1	.7850
Waterbuck	1	.4065		—	
Hippopotamus	1	.4265		71	
Buffalo	2	.4354			
Peccary	1	.4374			
Goat	1	.4547			
Axis deer	1	.4618			
Hartebeest	1	.4630			
Jersey cow	5	.4650			
Impala	2	.4672			
Holstein bulls	3	.4732			
Bushbuck	1	.4845			
Buffalo	1	.4928			
Impala	2	.4954			
White-tailed deer	1	.5225			
Bushbuck	1	.5322			
Caribou	3	.5755			
	1,080				

for the horse group is considerably higher than that of the Bos genus.

In connection with the relative standing of the various animals, it is interesting to note that the four caribou from the far North stand above the average for the even-toed group and higher even than the average established for the odd-toed animals.

In contrast to this relatively high degree of development of the carnivore and ungulate brain is the fish brain, as shown in Table 4.

TABLE 4
FISH BRAIN

Name	No.	Brain value
Eel and Jewfish	2	.0077
Salmon	5	.0123
Trout	8	.0234
Codfish	7	.0295
Shark	4	.1605

A curious finding in this connection is the high position of the cartilaginous fishes like the shark compared to that of the bony fishes. The salmon and the trout, in spite of their close relationship, show a tremendous difference in the matter of their degree of brain development. One difficulty encountered in evaluating the fish brain is the determination of the adult stage of a fish. If sexual maturity is taken as a criterion, great body weight variations appear in a given species even though only sexually mature specimens are chosen.

Curiously, the reptile and the amphibian brain, as already indicated, stand on a lower cephalization level than do the fishes. Of the reptiles, the snakes stand well toward the bottom of the list, while the alligator, turtle, lizard, gila monster, and horned toad stand at the opposite extreme. Table 5 gives a summary of the relative standing of the various types of reptiles.

TABLE 5
REPTILE BRAIN

Name	No.	Brain value
Snakes	35	.0099
Turtles	66	.0101
Lizards	17	.0180
Alligators	4	.0206
Horned Toads	3	.0223
Gila Monster	1	.0248

The average brain coefficient for the shrew, a representative insectivore, is .07439. The mole, although belonging to the same group, stands on a much higher level of brain development, the value being .1550. As a matter of fact, this animal is on the same level as are the rodents. The highest level of cephalization among the rodents is reached in the squirrels, the average value for 12 red squirrels being .2710. Four specimens taken at the very northern limit of the range

of this animal, at the margin of the tree line near Churchill, Canada, gave a value of .2813 for this coefficient.

Table 6 represents a summary of the brain values for the rodent groups.

TABLE 6
RODENT BRAIN

Name	No.	Brain value
Insectivores		
Shrews	68	.0743
Mole	1	.1550
Rodents		
Meadow Mouse	218	.1198
White Rabbits	22	.1440
Guinea Pigs	122	.1623
Arctic Hares	4	.2224
Squirrels, red, local	8	.2659
Squirrels, red, Churchill, Canada	4	.2813

The average cephalic coefficient for 175 adult birds taken from our records is .1855. This throws little light, however, on the variations of the coefficient within the group. It appears that brain size is correlated with flying ability, i.e., with the energy required to place and maintain a heavier than air body in flight, and perhaps with intelligence as well. Thus, the brain value for the common white Orpington fowl, which has lost its power of flight, stands at a level even lower than that of the ostrich. The value for the guinea fowl, partridge, leghorn fowl, and bustard lie in close proximity to that for the Orpington and the ostrich. The values for the pheasant, pigeon, and goose run somewhat higher. The brain values for the small flyers range from .1594 to .2129. At the top of the list is the crow with a coefficient of .5067, and fourth from the top, the horned owl, with a coefficient of .2989.

Table 7 summarizes some of these findings.

The brain coefficient of the primates excluding the human being averages .8709 for 449 specimens of Old and New World monkeys. The lowest value is found for the African lemur which stands at a level of .3866. The chimpanzee, the macaque, and the red and black spider monkeys stand nearest man on the list. Between these extremes is found a variety of Old and New World forms. In comparison with these primates, man stands on a high level of brain development, namely, at 3.625.

TABLE 7

Name	No.	Brain value
White Orpington Fowl	1	.0552
Ostrich	1	.0742
Ptarmigan	1	.0789
Partridge	1	.0836
Bustard	1	.0852
Humming Bird	1	.0862
Pheasant	1	.1009
Red Throated Loon	1	.1159
Pigeons	4	.1227
Small Flyers	153	.1856
Pelican	2	.2245
Highest 7 birds (without crow)	7	.2623
Crow	1	.5067

Table 8 shows the position of some of these adult primates in order of increasing cephalization.

TABLE 8

Name	No.	Brain value
African Lemur	1	.2881
Howler Monkeys	44	.4551
Marmosets	52	.4806
Ring-tail Lemur	1	.5867
Humboldt Monkeys	1	.8365
Baboon	1	.8465
Red and Black Spider	111	.8511
Macaque Rhesus	11	1.1203
Chimpanzee	3	1.2809
Human	11	3.6250

Our dissections include eight cetacea. Six were white whales, one a porpoise, and one a blue whale.

Whatever the origin of this group may have been, whether ungulate or carnivore, they have far outstripped all other animals save man in the size of the cephalization coefficient. The average value for the group is 2.220.

If brain size were correlated directly with intelligence, the cetacea should be the most intelligent of all animals excepting man, since the rate of their brain growth carries them far beyond the level achieved by carnivores and ungulates.

Apparently this great brain size is correlated with the water habitat of the cetacea. They are warm-blooded animals, and their heat loss, in spite of the protection given by blubber and fat, is large. Loss of appendages would of itself probably lead to a lesser cephalization, yet we

find them with enormous brains. As shown in our unpublished data, basal metabolism and brain size appear related in the ratio of one gram of brain for 12.11 calories in 24 hours in the vertebrates generally, with the exception of primates. This same principle appears to apply here.

Table 9 shows the cetacean cephalization values.

TABLE 9

Name	No.	Brain value
Blue Whale	1	1.711
White Whale	4	2.053
White Whale	2	2.550
Porpoise	1	2.737

C. Thyroid Scale

The thyroid gland shows greater irregularities in actual size as well as in histological appearance than do any of the other glands studied. Seasonal variations associated with climatic changes, geographical variations associated with the iodine content of the food and water, age variations, size variations associated with brain size, condition of the animal, and pregnancy all play a part in determining thyroid size and histological appearance.

In spite of these factors, certain regularities emerge when an extensive survey of the gland is made.

Table 10 indicates that animals exhibit definite levels of thyroidization just as they show differences in cephalization. Figure 4 sets forth these relationships. A comparison of Figure 4 with Figure 3,

TABLE 10

Name	No.	Average thyroid value
Fish	86	.1081
Bullfrogs	6	.1803
Reptiles	187	.3566
Birds	469	.3056
Insectivores and Rodents	508	.3436
Ungulates		
Odd-toed	89	.4201
Even-toed	1219	.5393
Carnivores		
Cat-like	39	.3870
Dog-like	32	.4804
Primates	126	.6580
Seals	14	.9212
Humans	11	3.4450
Cetacea	8	1.2230

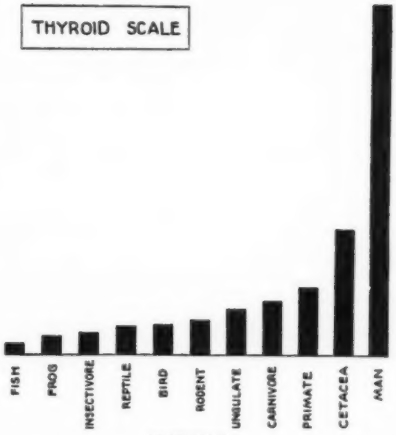

FIGURE 4
DEGREE OF THYROIDIZATION EXPRESSED IN TERMS OF "*b*"

in addition to showing the relative position of the various groups, reveals the similarity between the rise of the thyroid and rise of the brain. Thus, man, the cetacea, the primate, the carnivore, and the ungulate fall into the same relative position in both figures.

The fish with a thyroid gland value of .1081[1] stands at the foot of the vertebrate group with respect to degree of thyroid development, while man stands at the top with a value of 3.445. Between these two extremes are ranged the remaining back-boned animals as indicated in Table 10.

Bony fishes, of which we have 78, have an average thyroidization coefficient of only .0844 compared with .3390 for the sharks. The latter, as already pointed out, also possess a higher brain coefficient.

TABLE 11

Name	No.	Thyroid value
Bony Fishes	78	.0844
Cartilaginous Fishes	8	.3390

The average thyroid value for 187 reptiles was .3566. When separated into their natural divisions, the reptilian values are as given in Table 12.

[1]The actual calculated value for the thyroid and adrenal glands has been multiplied by 1000; the heart factor, by 10.

TABLE 12

Name	No.	Thyroid value
Turtles	66	.3003
Lizards	77	.3682
Horned Toads	5	.4452
Snakes	32	.4465
Alligators and Crocodiles	6	.4732
Gila Monster	1	.8229
	187	

The birds included in this thyroid gland study number 403. Of these 200 were growing leghorn fowls ranging in age from 6 to 136 days. The average thyroid values for these growing chicks range from .1456 to .2103 to an age of 62 days; when the thyroid seems to experience a sudden spurt of rapid growth. After 84 days it ranges from .2998 to .5500. In the four adult laying hens the average was higher than in any other birds.

TABLE 13

Name	No.	Thyroid value
Leghorns to 62 days	120	.1742
Small Flying Birds	178	.2961
Birds of Prey	12	.3620
Leghorns over 62 days	80	.3926
Poor Flyers	9	.4111
Leghorns, Adult (egg laying strain)	4	.5500

Flying birds ranging in body weight from 20 to 100 grams possessed an average thyroid coefficient of .2061 while for 12 birds of prey, including such diverse forms as the Man-o-War bird, the tawny eagle from Africa, various species of hawks, and horned owl, the average value was .3620.

The insectivores and the rodents show a wide range of variation

TABLE 14

Name	No.	Thyroid value
Insectivores		
Shrews	68	.2155
Rodents		
Mice	246	.2586
Squirrels	9	.2766
Guinea Pigs	122	.4172
Chipmunks	2	.4172
Rabbits. Domestic	22	.7228

in thyroidization as shown by Table 14. The domestic rabbit shows the highest values, a fact which may be associated with domestication. We have observed that in captivity the thyroid glands of most wild animals tend to enlarge. In the case of the domestic rabbit, it is possible that other factors beside restraint bring about an enlarged gland.

For the ungulates the values given in Table 15 speak for themselves.

TABLE 15

Name	No.	Thyroid value
Even-toed Ungulates		
Cows:		
Hereford	7	.3365
Jersey	217	.5214
Holstein	200	.5620
Ayrshire	44	.5643
Miscellaneous	71	.5715
Guernsey	62	.5716
Aberdeen Angus	1	.7303
Average	602	.5465
Bulls:		
Jersey	225	.5940
Holstein	206	.5950
Average	431	.5948
Steers	33	.5192
African Buffalo	2	.4376
Caribou	3	.4846
Other Even-toed Ungulates	48	.4833
Odd-toed Ungulates		
Guatemala Pony	2	.2668
Geldings	13	.3836
Horses, Female	42	.5108
Horses, Male	11	.5211
Zebra, Male	2	.6285
Shetland Pony, Male	1	.6908
Guatemala Burro	1	.6918
Panama Mules	5	.7107
Elephant	1	1.7000

The elephant (a sub-ungulate) has the largest thyroid gland coefficient; the mule stands second. The Guatemala horse is lowest in rank. The milk cow with an average of .5475 has a slightly larger gland than the mare at .4108. The bull with a thyroid value of .5948 has a relatively larger gland than the stallion at .5211. Castrated cattle, horses, and pigs stand at a lower level of thyroidization than do normal animals of the same species. The wild even-toed animals are on a lower level than are the domesticated animals.

The carnivorous animals fall into three natural divisions, the cat-like, the dog- or bear-like, and the aquatic forms. Their degree of thyroidization is indicated in Table 16.

TABLE 16

Name	No.	Thyroid value
Cat-like Carnivora	39	.3870
Dog- and Bear-like Carnivora	32	.4804
Seals and Walruses Carnivora	14	.9218

Great individual variations occur in the thyroid gland of this group and the common presence of goiter made it impossible to evaluate a great deal of this material. As a group, the carnivores, with exception of those which have taken to the water, stand on a lower thyroid level than do the ungulates.

Considering the interrelationship which exists among the primates, they show a remarkable degree of variation in the size of the thyroid gland. The gorilla, to judge from our one example, stands at the opposite extreme from man in this respect. So far as thyroid coefficients are concerned, the gorilla is next to the tiny African lemur, one of the smallest of the primates. Between these extremes is a variety of Old and New World monkeys. The chimpanzee (two wild specimens taken in the Great Budonga Forest in Africa) shows a higher thyroid value than does the gorilla, although neither of these groups indicate similarity to man in this respect. The thyroid gland of man stands at a level of development which is higher than that found in any other group. The average value of these adult primates was .6363, excluding man, where the average value was 2.9450. Table 17 is a résumé of the calculated values for the primate thyroid gland.

TABLE 17

Name	No.	Thyroid value
Gorilla	1	.1517
African Lemur	1	.1823
Baboon	1	.2415
Grey and Vervet Monkeys	7	.3071
Humboldt	1	.3487
Black Howler	4	.3570
Marmoset	2	.3720
Red Spider	24	.5125
Ring-tailed Lemur	1	.5315
Chimpanzee	2	.5561
Macaque Rhesus	8	.5850
Black Spider	17	.6536
Yellow Titi	6	.7601
Human	12	2.9450

Next to man in thyroidization is the cetacean group. As Table 18 shows, the average value for the whale and the porpoise is 1.7166.

TABLE 18

Name	No.	Thyroid value
Porpoise	1	.3543
White Whale, Female	2	2.1730
White Whale, Male	4	2.0670
Blue Whale	1	.7649

This high degree of thyroidization appears associated with a large brain, as is seen in Figures 3 and 4. Large brain, in turn, appears correlated with the aquatic habitat of this group. This applies to aquatic carnivora, e.g., seals and walruses as well. Table 19 shows that

TABLE 19

Name	No.	Brain value	Thyroid value
Seals and Walruses	14	.8051	.9218
Primates (without man)	449	.8709	.6363
Whales and Porpoises	8	2.2250	1.7166
Man	12	3.6200	2.9450

the walrus and seal group stand third in thyroidization and fourth in cephalization. This evidence indicates that as the brain goes, so goes the thyroid.

D. The Adrenal Gland

The fish does not possess an adrenal gland, but it does have an inter-renal body which is the homologue of the adrenal cortex in the land vertebrates. The adrenal medulla in the fish is represented by scattered chromaffin cells. We attempted to collect and weigh some of these cell clusters. The average of six such estimations gave an average adrenal value of .3078. In comparison this value is approximately the same as the average for the entire gland in the reptile, which was .2930 for 167 animals. When broken down into their natural subdivisions, these adrenal values varied as shown in Table 20 and Figure 5.

TABLE 20

Name	No.	Adrenal value
Turtles	66	.2377
Gila Monster	1	.2496
Lizards	71	.3639
Alligators and Crocodiles	12	.3676
Horned Toads	3	.5358
Snakes	14	.8168

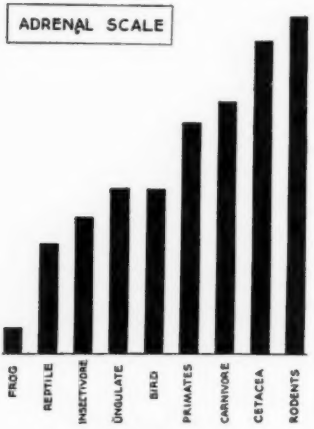

FIGURE 5
RELATIVE DEGREE OF ADRENALIZATION IN TERMS OF "*b*"

Just what the physiological significance of the high degree of adrenalization in the snake is, we cannot state, although it would appear to be correlated with its ability to mobilize energy as rapidly as does the warm-blooded animal. The lizard, however, a quick and agile creature, shows no corresponding adrenal factor.

The adrenal values observed in the bird are indicated in Table 21.

TABLE 21

Name	No.	Adrenal value
Guinea Fowl, Goose, Partridge, etc.	7	.3603
Common Fowl	4	.3807
Small Flyers	185	.4218
Birds of Prey	10	.4930
Large Flyers	13	.5158
Ostrich	1	.9631

The partridge-guinea fowl-pheasant-goose group appear low in comparison with the remaining birds. The ostrich has the highest adrenal value, although histological examination reveals only a small amount of medullary tissue. Large flyers like the stork, bustard, and crane stand second with birds of prey third.

Taken as a group, the even-toed ungulates, numbering 1212, have lower adrenal values than the odd-toed group. The wild ungulates

show a value of .4071, while the domestic hogs, the warthog, and the peccary give a value of .2346. The size of the adrenal gland in castrate and in normal hogs does not differ materially from that of the normal animal.

When these grass eaters are divided into natural groups, the values run as in Table 22.

TABLE 22

Name	No.	Average
Even-toed Ungulates		
Hogs, Warthog, etc.	121	.2346
Cows	602	.3480
Bulls	426	.3715
Steers	33	.4327
Wild Ungulates	30	.4071
	1212	
Odd-toed Ungulates		
Thoro. Stallion (Penn.)	1	.3122
Thoro., Male	8	.3398
Burros	2	.3486
Horses, Male, Misc.	3	.3866
Geldings, Mixed	10	.4892
Horses, Female, Mixed	35	.4985
Thoro. Stallion (Eq.)	1	.5099
Thoro., Female	5	.5197
Shetland Pony	1	.5289
Zebras, Male	4	.5895
Guatemala Ponies	2	.6431
Mules, Panama	7	.7552
	79	
Elephant	1	1.1450
	1291	
Average of all ungulates—.3590		

As in the case of the brain, the elephant again stands on an entirely different level than do the true ungulates, the adrenal value being 1.1450.

The average adrenal coefficient value is considerably higher in the carnivores than in grass eating ungulates. Average values for 90 carnivores were .6624 compared with .3590 for ungulates.

The values for the various types of carnivora show a difference in pattern as indicated by Table 23. Seals and walruses stand on a very low level of adrenalization, the value established for them is only .2694. Cat-like animals show the highest values in the group. Two wild African lions show values higher than either the dog- or the remaining cat-like group.

TABLE 23

Name	No.	Adrenal value
Walruses and Seals	11	.2694
Dog-like	34	.3629
Local and African dogs	77	.4463
Husky Dogs, Greyhound, and Northern Fox	7	.5657
Cat-like	25	.8406
	86	

To judge from the high degree of variation in the adrenal glands as well as in brain size, each group of primates appears to be a law unto itself where these glands are concerned (Table 24). Adrenal

TABLE 24

Name	No.	Adrenal value
African Lemur	1	.3624
Grey and Vervet Monkeys	7	.4316
Humboldt Monkeys	1	.5664
Black Howler	30	.5750
Baboons	2	.6807
Macaque Rhesus	11	.7308
Marmosets	16	.7512
Red Spiders	83	.7582
Negro—normal	4	.7672
Chimpanzees	2	.7694
Black Spiders	17	.8004
White—normal human	7	.8217
White male (path.) human	11	.8440
White female (path.) human	1	.9058
Gorilla	1	.9638
White Face Monkeys	23	1.0774
Ring-tailed Lemur	1	1.2910
Brown Howlers	6	1.4030
Yellow Titi	66	2.3260
	274	

values range from .3624 in the tiny African lemur to 2.326 in the equally small South American yellow titi monkey. Man finds himself between chimpanzee and gorilla in this table. With exception of the gorilla, all higher ranking groups are New World monkeys.

The average value for the cetacea is .6643 which is considerably higher than the value established for aquatic carnivores (Table 25). The blue whale has an unexpectedly high adrenal value.

Insectivores and rodents, on the basis of actual gland ratios, exhibit the highest degree of development of the adrenal glands of any of the animals. Measured in terms of *"b"* values they fall more nearly

TABLE 25

Name	No.	Adrenal value
White Whales	6	.4190
Porpoise	1	.8989
Blue Whale	1	1.8950
	8	

in line with other groups. The shrews show much smaller adrenal gland factor than do the mice. The value for 69 of these animals is .3528.

The mice, considering their small body weight, are well supplied with adrenal glands, the adrenal value for the group averaging .5577 for 253 animals. Thirteen squirrels show a value of .8115, with 122 guinea pigs at 1.5771 (Table 26). This value appears entirely out of line with the smaller rodents.

TABLE 26

Name	No.	Adrenal value
Insectivores		
Shrew	69	.3528
Rodents		
Mice	253	.5577
Shik-shiks	8	.6029
Squirrels	13	.8115
Lemmings	4	.8964
Guinea Pigs	122	1.5771
	569	

E. The Heart

The heart reflects the activity pattern of the individual just as it mirrors the activity of the race. Application of the power formula to the heart reveals both of these characteristics. Thus, the heart of the fish is much smaller relatively than is the heart of the carnivore. This is an inbred difference related to the difference in vascularization of the musculature of the two orders. On the other hand, the heart of three outstanding thoroughbred stallions is larger relatively than that of the work horse or the thoroughbred mare. This, we believe, is in large measure an acquired characteristic, primarily the result of training, although inbred differences are not entirely ruled out in this case.

Measured in terms of the growth equation, the heart coefficients

stand in the relationship given in Table 27 and shown graphically in Figure 6.

TABLE 27

Name	No.	Average heart values*
Fishes	69	.0542
Bullfrogs	6	.0811
Reptiles	77	.0907
Rodents and Insectivores	485	.1328
Primates	223	.1561
Human (white normal male)	7	.2441
Birds	236	.2605
Human (Negro normal male)	4	.2703
Human (white path. males)	10	.2727
Ungulates	1119	.2951
Carnivores	72	.2952
Human (white female path.)	1	.3097
Cetacea	7	.3722
	2316	

*Values multiplied by 10

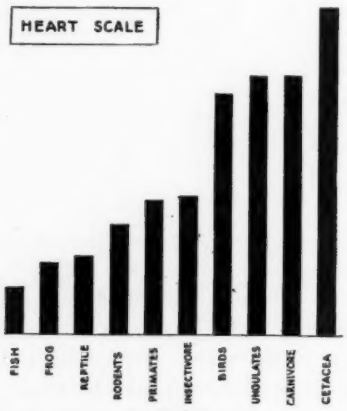

FIGURE 6
GRAPHIC REPRESENTATION OF CARDIAC "*b*" COEFFICIENTS

Fishes show the lowest heart value of any of the animals examined. This is probably due in part to their aquatic habitat, as well as to their low degree of vascularization. Within the group itself differences appear. Thus cartilaginous fishes show the highest, while whitefish, perch and pike have the lowest cardiac coefficients. Table 28 shows the relative standing of the fish group.

TABLE 28

Name	No.	Heart value
Whitefish	6	.0431
Perch and Pike	11	.0442
Mixed Ocean Fish	18	.0486
Trout	13	.0492
Codfish	7	.0529
Salmon	8	.0793
Cartilaginous	6	.0959

Frogs with a value of .0811 are second lowest in cardiac values, although lizards have a lower value than frogs.

The reptiles as a group are third in line as to heart value. Turtles, snakes, and the gila monster stand considerably above the alligators and the lizards. This fact might be foretold by examining the amount of blood in these groups. These three types possess a greater blood supply than do the others. Table 29 indicates the calculated values for this group.

TABLE 29

Name	No.	Heart value
Lizards	52	.0682
Horned Toads	5	.0713
Alligators and Crocodiles	6	.1099
Turtles	6	.1532
Snakes	7	.1855
Gila Monster	1	.2065
	77	

The rodents and insectivores appear next to reptiles in cardiac values. Mice are at the foot of this group with shrews considerably above them, while the arctic ground squirrel or shik-shik heads the group.

TABLE 30

Name	No.	Heart value
Mice	229	.1164
Mole	1	.1193
Guinea Pigs	122	.1290
Shrews (Insectivores)	68	.1598
Rabbits	30	.1645
Agouti	10	.1693
Squirrels	12	.1737
Lemmings	5	.1765
Shik-shiks	8	.1800
	485	

Average for the Insectivores and Rodents, 485 animals—.1328
Average for the Rodents, 417 animals—.1284

Birds appear next in degree of cardiac development. The canary at the foot of the bird list has a value of .1932, while, with the exception of the ostrich, the tiny humming bird shows the highest value—.3032.

Large birds of prey and heavy flyers like stork, goose, and bustard are approximately at the same cardiac level as small active flyers, the latter showing but a very slight increase. In fact, birds show a remarkably similar cardiac value with exception of the ostrich, humming bird and canary, as is shown by Table 31.

TABLE 31

Name	No.	Heart value
Canaries	2	.1932
Birds of Prey	13	.2489
Poor Flyers	36	.2540
Small Flyers	184	.2595
Humming Bird	1	.3032
Ostrich	1	.3557
	236	

The primates exhibit a wide range of heart coefficients extending from .0664 for the brown howler monkey to .2441 for the normal white human male. The human being ranks high in the primate group, ranging just under the chimpanzee. While the primate values are lower than those established for the outstanding ungulates, carnivores and cetacea (Figure 6), the value for man is about midway between

TABLE 32

Name	No.	Heart value
Brown Howlers	6	.0664
Night Monkeys	4	.0979
Black Howlers	28	.1021
Macaque Rhesus	11	.1201
Marmosets	8	.1342
Grey, Vervet and Sykes Monkeys	10	.1408
Ring-tailed Lemur	1	.1454
African Lemur	1	.1558
Yellow Titi	60	.1585
Red Spiders	63	.1629
Baboon	1	.1839
White Face Monkeys	14	.2003
Human	7	.2441
Humboldt Monkey	1	.2621
Chimpanzees	2	.2677
	223	

the values established for fishes and cetacea. Calculations for 223 adult primates show an average heart coefficient of .1561. Apparently the normal negro male ranks slightly higher than the normal white male, perhaps reflecting differences in work habit.

The carnivore and the ungulate averages for the heart factor are virtually identical, although individual variations run high. In the case of the carnivore we have heart records on 72 adult animals; for the ungulates we have records on 1,119 adults.

Table 33 indicates the heart record for the carnivora. The cat-like

TABLE 33

Name	No.	Heart value
Cat-like	33	.2230
African Lions	2	.3306
Dog-like	33	.3310
Seals and Walruses	6	.4965
	72	

animals stand on a considerably lower level than do the dog- and bear-like animals. Heart values for two African lions with a value of .3306 equals that for the dog-like group. Towering above all are the aquatic mammals, which seemingly show a contradictory heart value in view of the fact that they are supported by the water in which they live and that they have all but lost their appendages. These aquatic animals, however, are the most highly vascularized of all animals with the exception of the porpoise and whale, and this appears to be the controlling factor in determining their heart coefficient.

Among even-toed ungulates, the domestic pig is lowest in the heart scale, with warthog and peccary next in position. Domestic cattle stand below their wild relatives. In the odd-toed groups the situation appears reversed, as the tapir stands below the domesticated animals and the zebra stands below the thoroughbred horse. The rhinoceros, however, stands well in line with the horse group. Three thoroughbred stallions bred for stamina, endurance, and speed top the list as illustrated in Table 34.

Heart values for porpoise and white whales give a clue to the high degree of their vascularization. The average for six white whales and one porpoise is higher than in any other group save certain of the ungulates (Table 35).

TABLE 34

Name	No.	Heart value
Even-toed Ungulates		
Hogs	119	.1691
Peccary and Warthog	6	.2507
Steers	18	.2829
Bulls	426	.2884
Cows	495	.3142
Wild Ungulates	22	.3577
Northern Caribou	3	.4298
Odd-toed Ungulates		
Tapir	2	.3081
Burro	1	.3269
Zebra, Female	1	.4391
Zebras, Male	4	.4736
Horses, Female	7	.4777
Rhinoceros	1	.4800
Horses, Male	11	.5482
Stallions, thoroughbred (Pennant, Equipoise and Hunt Club)	3	.6772
	1119	

TABLE 35

Name	No.	Heart value
Porpoise	1	.3071
White Whales	6	.3831
	7	

F. Conclusions

The data and calculations presented in connection with the degree of brain, thyroid, adrenal, and heart developments in various animal groups points to an underlying principle of growth and size increase which, apparently, is best expressed by the equation $Y = bX^k$.

It is possible to set up a scale of being based on the numerical values of "*b*" as calculated for brain, thyroid, adrenal glands, and heart.

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